Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Preliminary Work Plan

Registration Review: Initial Docket Case Number 0350

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TERMS, ABBREVIATIONS AND SYMBOLS

AD	Antimicrobials Division
ADBAC	alkyl dimethyl benzyl ammonium chloride
A.I. or a.i.	active ingredient
aPAD	acute population adjusted dose
ASRI	activated sludge respiration inhibition
atm-m^3/mole	atmospheric pressure-cubic meter per mole
BCF	bioconcentration factor
°C	degrees Celsius
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations
CHO	Chinese hamster ovary
CMA	Chemical Manufacturers Association
CO_2	carbon dioxide
COC	concentration-of-concern
cPAD	chronic population adjusted dose
DCI	data call-in
DDAC	Didecyl Dimethyl Ammonium Chloride
EC_{50}	median (or 50 percent) effect concentration
EC_{05}	5 percent effect concentration
ECOTOX	ECOTOXicology
EDI	estimated daily intake
EDSP	Endocrine Disruptor Screening Program
E-FAST	Exposure and Fate Assessment Screening Tool
EPI Suite	Estimation Program Interface Suite
EPA	Environmental Protection Agency
FCN	food contact notification
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FWP	Final Work Plan
g/mol	grams per mole
GLN	guideline number
HEC	Human Equivalent Concentration
HPV	high production volume
IDS	Incident Data System
Koc	organic carbon normalized soil-water partition coefficient
Kd	soil-water partition coefficient
Kow	octanol-water partition coefficient
LC_{50}	median (or 50 percent) lethal concentration
LD_{50}	median (or 50 percent) lethal dose
LOAEC	lowest-observed-adverse-effect-concentration
LOEC	lowest-observed-effect-concentration
LOAEL	lowest-observed-adverse-effect-level
Log K_{ow}	logarithm of the octanol-water partition coefficient
µg	microgram
ml/g	milliliter per gram
mg/kg	milligram per kilogram

mg/kg/day	milligram per kilogram per day
mg/L	milligram per liter
mm Hg	millimeter of mercury
MOE	margin of exposure
MRID	Master Record Identification Number
MRL	maximum residue limit
N/A	not applicable
nm	nanometers
NOAEC	no-observed-adverse-effect-concentration
NOAEL	no-observed-adverse-effect-level
OCSPP	Office of Chemical Safety and Pollution Prevention
OECD	Organization for Economic Co-operation and Development
OPP	Office of Pesticide Programs
PAD	population adjusted dose
PAI	pure active ingredient
PDM	Probabilistic Dilution Model
%	percent
PC Code	Pesticide Chemical Code
PCF	pounds per cubic foot
pH	power of hydrogen or power of the concentration of the hydrogen ion
PHED	Pesticide Handler's Exposure Data
PIS	primary irritation score
pKa	power of the acid dissociation constant or negative base-10 logarithm of the acid dissociation constant of a solution
ppb	parts per billion
ppm	parts per million
PWP	Preliminary Work Plan
PWR	potable water rinse
QSAR	quantitative structure-activity relationship
RDDR	Regional Dose Deposition Ratio
RED	Reregistration Eligibility Decision
SAR	structure activity relationship
SF	safety factor
SSTS	Section Seven Tracking System
TEP	typical end-use product
TGAI	technical grade active ingredient
TMDL	total maximum daily loads
UF	uncertainty factor
UV/VIS	ultraviolet/visible light absorption
% w/w	percent weight per weight.
WP	wettable powder
WWTPs	wastewater treatment plants
USDA	United States Department of Agriculture

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1 Introduction

This document is the United States Environmental Protection Agency's (USEPA, EPA or "the Agency") Preliminary Work Plan (PWP) for the Alkyl Dimethyl Benzyl Ammonium Chloride chemical case, herein referred to as ADBAC. The PWP document explains what EPA's Office of Pesticide Programs (OPP) knows about ADBAC, highlighting anticipated data and assessment needs, identifying the types of information that would be especially useful to the Agency in conducting the review, and providing a screening-level dietary risk assessment and an anticipated timeline for completing ADBAC's review.

The registration review process was designed to include a public participation component to solicit input from interested stakeholders. The Agency intends, by sharing this information in the docket, to inform the public of what it knows about ADBAC and what types of new data or other information would be helpful for the Agency to receive as it moves toward a decision on ADBAC. The Agency encourages all interested stakeholders to review the PWP and to provide comments and additional information that will help the Agency's decision-making process for this chemical.

1.1 Statutory and Regulatory Authority

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides distributed or sold in the United States generally must be registered by the USEPA based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at http://www2.epa.gov/pesticide-reevaluation.

The Agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The regulations governing registration review begin at 40 CFR 155.40. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial comment period, the Agency will develop and commit to a Final Work Plan (FWP) and anticipated schedule for the ADBAC case.

1.2 Case Overview

The docket for ADBAC (case #0350) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2015-0737. Documents associated with this registration review can be viewed in this docket. Tables 1 and 2 below summarize the issues relevant to this registration review case and the anticipated registration review schedule.

Table 1 – Anticipated Risk Assessments for Registration Review

Risk Assessment	Assessment Necessary to Support Registration Review	Date of Most Recent Assessment	Type of Assessment Required (New/ Updated)	Data Anticipated as Needed* (See Table 14 for details)
Dietary (food)	Yes	August 2006	Updated	Residue Data
Dietary (drinking water)	Yes[1]	N/A	New	Activated Sludge Sorption Isotherm (ASSI), WWTP Biodegradation, and Activated Sludge Respiration Inhibitor (ASRI)
Occupational Handler	Yes	2006	Updated	None
Residential Handler	Yes	2006	Updated	None
Occupational Post Application	Yes	2013	Updated	None
Residential Post Application (Antimicrobial)	Yes	2006	Updated	Post Application Inhalation Exposure
Residential Post Application (Conventional)	Yes	2006	Updated	Turf Transferable Residue Dissipation
Aggregate	Yes	August 2006	Updated	None
Cumulative	No	N/A	None	None
Tolerance Review	Yes	2006	Updated	None
Ecological – antimicrobial and conventional uses	Yes	2006[2]	Updated	Toxicity data for aquatic plants, benthic invertebrates, and honey bees.

N/A = Not applicable
[1] If the Agency receives environmental fate data which demonstrate strong sorption to activated sludge and a lack of toxicity to WWTP microorganisms, the Agency would not anticipate conducting a drinking water risk assessment.
[2] Antimicrobial uses assessed in the RED were once-through cooling towers and wood preservatives (antisapstain use).
***** Table 1 is a summary of the anticipated risk assessments and data needs for registration review. For data called in through the post-Reregistration Eligibility Decision (RED) Data Call-In (DCI), see Table 15.

Table 2 – Anticipated Registration Review Schedule

Anticipated Activity	Target Date*	Completion Date
Phase 1: Opening the Docket		
Open Docket and 60-Day Comment Period for Preliminary Work Plan	2016-09	2016-09
Close Public Comment Period	2016-11	
Phase 2: Case Development		
Issue Final Work Plan	2017-03	

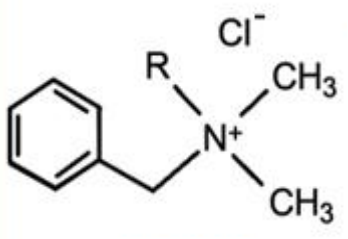
Issue Data Call-In (DCI)	2018-03	
Receive Data to be Considered in Risk Assessment	2020-03	
Open 30-Day Public Comment Period for Preliminary Risk Assessment(s)	2021-09	
Close Public Comment Period	2021-10	
Phase 3: Registration Review Decision and Implementation		
Open 60-Day Public Comment Period for Proposed Decision	2022-03	
Close Public Comment Period	2022-05	
Issue Final Decision	2022-09	
Begin Post-Decision Follow-up	2022-09	
Total (years)	6	

*The anticipated schedule will be revised as necessary (*e.g.*, need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

1.3 Chemical Identification and Properties

Table 3 and 4 present the chemical and physical properties of the active ingredient to be assessed in case 0350: ADBAC. The ADBAC chemical case is composed of 19 compounds (PC Codes: 069104, 069105, 069106, 069107, 069119, 069137, 069140, 069141, 069175, 069184, 128928, 069171, 069154, 069111, 069125, 069122, 069167, 069195 and 129012). The Agency will use alkyl (40% C_{12}, 50% C_{14}, 10% C_{16}) dimethyl benzyl ammonium chloride (PC code 069105) as the model compound because this active ingredient has the highest number of active registrations and therefore, is expected to be the most representative compound for this case (EPA, 1994).

Table 3 – Chemical Identification of ADBAC

Chemical Name	**ADBAC**
Chemical Classification	Quaternary Amines
PC Code	069105
CAS Number	68424-85-1
Molecular Formula	$RC_9H_{13}NCl$ R= n-alkyl (C_{12} 40%, C_{14} 50%, C_{16} 10%)
Molecular Weight (grams/mole)	377.83
Molecular Structure	

The ADBAC product chemistry and physical property information relevant to risk assessment is summarized in Table 4, and details of the environmental fate information are discussed in Appendix B.

Table 4 – Physical-Chemical Properties for ADBAC (PC Code 069105)

Guideline No.	Parameter	Value	Source (MRID unless specified)
830.7000	pH	7.59	44467403
830.7050	UV/visible Absorption	None in 290-800 nm range	47398502
830.7300	Density (g/cm^3 at 25 °C)	0.9429	44467403
830.7370	Dissociation constant (pKa)	N/A	49740501
830.7550	Octanol-water partition coefficient at 25 °C (Log K_{ow})	3.91	EpiSuite v.4.11
830.7840	Solubility in water (mg/L)	10,000	EpiSuite v.4.11
None	Boiling Point (°C)	560.84	EpiSuite v.4.00
830.7950	Vapor pressure (mmHg) at 25 °C	$3.53x10^{-12}$	EpiSuite v.4.00
None	Henry's law constant at 25 °C (atm-m^3/mol)	$1.34x10^{-11}$	EpiSuite v.4.11

atm-m^3/mol = atmosphere cubic meter per mole; °C = degrees Celsius; mg/L = milligrams per liter; mmHg = millimeters of mercury

1.4 Use/Usage Description

1.4.1 Registrations

There are 714 EPA-registered products that contain ADBAC as an active ingredient (a.i.), 711 of which are antimicrobial registered products and 3 that are conventional registered products. The 3 conventional registered products (EPA Registration Numbers 1021-2559, 9688-314 and 9688-317) are insecticides co-formulated with antimicrobial active ingredients. Additionally, of the 711 antimicrobial-registered products, 24 products have conventional use sites. These 24 products include 14 technical products and 10 end use products. Eight of these end use products (EPA Registration Numbers 10324-94, 10324-99, 55364-5, 58044-3, 66784-1, 66784-2, 84115-1, and 87429-1) contain only antimicrobial ingredients and the conventional use sites include ornamental plants, ornamental trees, lawns and turf. The two other end use products (70385-3 and 70385-4) also contain insecticidal ingredients and are used on a wide variety of use sites to control insects and microorganisms.

Table 5 presents ADBAC chemical case's 19 structurally similar quaternary ammonium compounds (also known as QACs or quats) compounds, CAS numbers, ingredient names, and active registrations (at the time of ADBAC's PWP publication to the docket). The formulations include ready-to-use solutions, pressurized liquids, soluble concentrates, pellets/tablets, dust, aerosols, impregnated materials, and flowable concentrates. The product pesticide types include disinfectants, bacteriocides, bacteriostats, fungicides, fungistats, virucides, sanitizers, microbicides, microbiostats, algaecides, tuberculocides, antimicrobials, water purifiers, miticides, and slimicides. Several of ADBAC's products contain multiple active ingredients including but not limited to: other ADBAC chemical case compounds, Didecyl Dimethyl

Ammonium Chloride (DDAC) chemical case compounds[1], glutaraldehyde, and pine oil. The three conventional registered products contain ADBAC chemical case compounds, DDAC chemical case compounds, plus any of the following active ingredients: cypermethrin, pyrethrins, and prallethrin.

Table 5 – Number of EPA Registered Products that contain ADBAC Sorted by PC Code

PC code	CAS Number	Ingredient Name	Number of active AD registrations as of 8/25/16[1]	Number of active RD registrations as of 8/25/16[1]
069104	53516-76-0	Alkyl (60%C_{14}, 30%C_{16}, 5%C_{18}, 5%C_{12}) dimethyl benzyl ammonium chloride	271	2
069105	68424-85-1	Alkyl (50%C_{14}, 40%C_{12}, 10%C_{16}) dimethyl benzyl ammonium chloride	329	1
069106	8001-54-5	Alkyl (50%C_{12}, 30%C_{14}, 17%C_{16}, 3%C_{18}) dimethyl benzyl ammonium chloride	2	0
069107	139-08-2	Alkyl (100% C_{14}) dimethyl benzyl ammonium chloride	4	0
069111	8045-21-4	Alkyl (50%C_{12}, 30%C_{14}, 17%C_{16}, 3%C_{18}) dimethyl ethylbenzyl ammonium chloride	13	0
069119	73049-75-9	Dialkyl (60% C_{14}, 30% C_{16}, 5% C_{18}, 5% C_{12}) methyl benzyl ammonium chloride	37	0
069122	121-54-0	Benzenemethanaminium, N,N-dimethyl-N-(2-(2-(4-(1,1,3,3-tetramethylbutyl)phenoxy)ethoxy)ethyl)-, chloride	11	0
069125	1330-85-4	Dodecylbenzyl trimethyl ammonium chloride	1	0
069137	68424-85-1	Alkyl (60%C_{14}, 25%C_{12}, 15%C_{16}) dimethyl benzyl ammonium chloride	9	0
069140	61789-71-7	Alkyl (61% C_{12}, 23% C_{14}, 11% C_{16}, 2.5% C_{18}, 2.5% C_{10}, trace C_8) dimethyl benzyl ammonium chloride	1	0
069141	68424-85-1	Alkyl (58%C_{14}, 28%C_{16}, 14%C_{12}) dimethyl benzyl ammonium chloride	23	0
069154	85409-23-0	Alkyl (68%C_{12}, 32%C_{14}) dimethyl ethylbenzyl ammonium chloride	203	2
069167	68956-79-6	Alkyl (60%C_{14}, 30%C_{16}, 5%C_{12}, 5%C_{18}) dimethyl ethylbenzyl ammonium chloride	2	0
069171	68989-01-5	Alkyl (50% C_{14}, 40% C_{12}, 10% C_{16}) dimethyl benzyl ammonium saccharinate	7	0
069175	68391-01-5	Alkyl (67%C_{12}, 25%C_{14}, 7%C_{16}, 1%C_{18}) dimethyl benzyl ammonium chloride	29	0
069184	68424-85-1	Alkyl (95%C_{14}, 3%C_{12}, 2%C_{16}) dimethyl benzyl ammonium chloride	16	0
069195	68391-01-5	Alkyl (41%C_{14}, 28%C_{12}, 19%C_{18}, 12%C_{16}) dimethyl benzyl ammonium chloride	1	0
128928	63449-41-2	Alkyl (67%C_{12}, 25%C_{14}, 7%C_{16}, 1%C_8, C_{10}, and C_{18}) dimethyl benzyl ammonium chloride	7	0
129012	61789-18-2	Alkyl (as in fatty acids of coconut oil) trimethyl ammonium chloride	1	0

[1] The registration review Didecyl Dimethyl Ammonium Chloride (DDAC) PWP chemical case (case number 3003) is located at http://www.regulations.gov in docket number EPA-HQ-OPP-2015-0740.

AD = Antimicrobials Division (responsible for antimicrobial products)
RD = Registration Division (responsible for conventional products)
[1] Several of ADBAC's products contain multiple active ingredients. As a result, many products are recorded more than once under multiple ADBAC PC Codes.

The individual exposure scenarios in ADBAC assessments are developed by summing the total percent of ADBAC active ingredients on a product's label.

1.4.2 Summary of Registered Uses

Table 6 presents a summary of the registered uses of ADBAC that will be assessed in this registration review. This table also includes the application methods.

Table 6 – ADBAC Registered Uses that will be Assessed During Registration Review

Use	Application Method	ADBAC Concentration Range/ Application Rate[1]
Agricultural Premises and Equipment		
Hard Surface Sanitizer/Disinfectant	Spray, Mop, Sponge, Wipe	200 to 16,000 ppm[2]
Hoof Trimming Equipment	Dip	625 to 2,800 ppm
Entryway Shoe Baths	Shoe Bath	350 to 2,000 ppm
Hatchery Rooms – Empty	Fog	1.1 to 3.8 %
Incubators and Hatchers - Occupied	Fog	919 ppm
Aquatic Areas		
Decorative fountains, pools and water displays (Algaecidal use)	Open pour	2 ppm
Commercial, Industrial, Institutional, Premises and Equipment		
Cadavers – Cleansing of Exterior Body Surfaces	Sponge, Towel, Brush	188 to 528 ppm
Hard Surface Sanitizer/Disinfectant	Spray, Mop, Sponge	100 to 16,000 ppm[2]
Commercial Laundry	Open pour	780 ppm
Drywall, trim and frame lumber	Spray	450 to 1,700 ppm
Garbage trucks and equipment	Spray	450 to 1,700 ppm
Painted Surfaces (Antimicrobial Paint)	Brush, Roller	5,200 ppm[3]
Soft Surface Deodorizer (Carpets)	Spray, Mop	450 to 1,700 ppm
Food Handling/Storage Establishments Premises and Equipment		
Hard Surface Sanitizer/Disinfectant	Spray, Mop, Sponge	200 to 16,000 ppm[2]
Egg Shell Sanitation	Spray	200 to 470 ppm
Dairies, beverage and food processing plants	Fog	0.34%
Human Drinking Water (Sanitization of Interior Hard Surfaces of Equipment and Tanks)		
Ice Machines, Water holding tanks, Reverse Osmosis (RO) units	Open Pour, Spray, Circulate in Place (CIP)	400 to 470 ppm
Industrial Processes and Water Systems		
Cooling Water Systems	Open pour	2 to 20 ppm
Oil and gas drilling and fracturing fluids	Open pour	2 to 500 ppm
Paper Mill Processing Water (Whitewater)	Open pour	0.5 to 100 ppm
Wastewater Systems	Open pour	50 to 250 ppm

Use	Application Method	ADBAC Concentration Range/ Application Rate[1]
Material Preservative		
Paper Products	Open Pour	600 ppm
Medical/Dental/Veterinary Premises and Equipment		
Hard Surface Sanitizer/Disinfectant Painted Surfaces (Antimicrobial Paint) Salon/Barber instruments and tools	Spray, Mop, Sponge, Wipe Brush, Roller Immersion	200 to 16,000 ppm[2] 5,200 ppm[3] 200 to 1,100 ppm
Residential and Public Access Premises		
Hard Surface Sanitizer/Disinfectant Humidifier Water (Evaporative Humidifiers Only) Exterior Surfaces (decks, walkways and patios) Painted Surfaces (Antimicrobial Paint) Waterbed Water	Spray, Mop, Sponge, Wipe Open Pour Spray Brush, Roller Open Pour	200 to 16,000 ppm[2] 7 to 510 ppm 740 to 17,000 ppm 5,200 ppm[3] 35 to 164 ppm
Swimming Pools and Spas		
Hard Surface Sanitizer/Disinfectant Pool and Spa Water Treatment	Spray, Mop, Sponge, Wipe Open Pour Liquid or Place Solid	200 to 16,000 ppm[2] 2 to 8 ppm
Wood Preservation		
Seasoned lumber (termite control) Fresh cut lumber (sapstain control) Existing wood shingle and shake roofs and siding	Pressure Treat/Double Vacuum Dip or Spray Brush or Spray	0.1 to 0.6 pcf 1.9 to 3.0% 0.5 to 3.0%
Conventional Uses		
Residential lawns and turf Commercial turf Golf course, greens and tees Nursery ornamentals Decorative fountains, pools and water displays (mosquito control)	Spot treatment (10 acre max) Spot treatment (10 acre max) Spot treatment (10 acre max) Spray or drench treatment Open pour	6.8 lbs a.i./Acre[4] 0.75 lbs a.i./Acre[5] 0.8 lbs a.i./Acre[5] 0.25 lbs a.i./plant 350 ppm a.i.

[1] The concentration ranges/application rates are based on the ADBAC content of the end use products. These rates do not include DDAC.
[2] The rate of 16,000 ppm is for products such as 74436-1 and 80346-1, which are two-part formulations. Part A contains 32,000 ppm ADBAC and is mixed in equal amounts with Part B, which contains hydrogen peroxide, to yield a solution containing 16,000 ppm ADBAC. The rate for all other labels is 200 to 5000 ppm.
[3] Only one product (64695-1) has this use.
[4] Limited to 6 treatments per year with a retreatment interval of 10 days.
[5] Limited to 6 treatments per year with a retreatment interval of 10 days, not to exceed 10 acres.

Some registered uses of ADBAC will be removed from EPA product labels in accordance with the Reregistration Eligibility Decision (RED)[2]. Labeling changes were specified as part of the risk mitigation measures outlined in the August 2006 ADBAC RED. "Table 13. The Labeling Changes Summary Table" in the ADBAC RED describes how language on labels containing ADBAC active ingredients should be amended. The registered use in Table 7 was not supported

[2] The ADBAC RED is located at http://www.regulations.gov in docket number EPA-HQ-OPP-2006-0339.

at the time of the RED and therefore, is one example of an ADBAC use that will be removed from EPA product labels through ADBAC's post-RED label review process, as noted in section 1.5.

Table 7 – ADBAC Registered Use that will be Removed from EPA Product Labels

Use	Application Method	Concentration Range/ Application Rate
Dairy Cows – Udder, flanks and teats[1]	Wash with Towel	72 to 100 ppm ai

[1]This use is included on two product labels (9768-12 and 1839-189). This use will be removed from EPA Reg. No. 9768-12 because it is not an EPA use. EPA Reg. No. 1839-189 will be voluntarily cancelled due to Stepan Company's ADBAC Product Specific Data Call-In (PDCI) 90 Day Response. This use is only one example of ADBAC uses that will be removed from the EPA product labels through ADBAC's post-RED label review process.

Registrants with products claiming mosquito control are required to submit efficacy data to the Agency, as this use will be assessed through the Agency's registration review process. According to 40 CFR 158.2160, efficacy data is required to be submitted to the Agency if a pesticide product bears a claim to control public health pests, including mosquitoes, that may directly or indirectly transmit diseases to humans. Therefore, the Agency reserves the right to require submission of efficacy data for all products containing ADBAC active ingredients with mosquito control claims.

1.4.3 Usage Information

Production volume data for the years 2011 through 2014 indicate that no more than 90 million kilograms (approximately 198 million pounds) of ADBAC are sold per year in the United States. Data for the years 2015 and 2016 were not used in this estimate since data collection is still in progress.

1.5 Regulatory History

In 1947, the first pesticide product containing an ADBAC active ingredient was registered in the United States. The oldest currently-registered product containing an ADBAC a.i. was registered in 1956 under PC Code 069105. These pesticides were classified as List A chemicals for which a registration standard was issued by EPA in 1985. When the list of active ingredients undergoing reregistration was published in 1989, 43 additional active ingredients were added to the reregistration case.

In 1988, the Agency issued PR Notice 88-2 outlining "Clustering of Quaternary Ammonium Compounds" where structurally similar quats were clustered into 4 groups as follows:

Group I: The alkyl or hydroxyalkyl (straight chain) substituted Quats

Group II: The non-halogenated benzyl substituted Quats (including hydroxybenzyl, ethylbenzyl, hydroxyethylbenzyl, naphthylmethyl, dodecylbenzyl, and alkyl benzyl)

Group III: The di- and tri-chlorobenzyl substituted Quats

Group IV: Quats with unusual substitutes (charged heterocyclic compounds).

ADBAC's chemical case was clustered into Group II and the Agency completed a Reregistration Eligibility Decision (RED) for ADBAC in August 2006. The post-RED Generic Data Call-Ins (DCIs) were issued in December 2014 and the post-RED Product Specific DCIs were issued in February and March 2015[3]. The RED specified label changes to mitigate human health and environmental risks and the Agency notes that there are existing labels not yet in compliance with these risk mitigation measures. Some of these mitigation measures would impact the risk assessment characterization for this registration review work plan, and the Agency is actively working to bring these labels into compliance.

A consortia was formed by ADBAC registrants to support the reregistration activities of the ADBAC chemical case. The consortia, the ADBAC Issues Steering Committee/Joint Venture, is comprised of the following registrants: Lonza Incorporated, Mason Chemical Company, and Stepan Company.

Since reregistration, several human health risk assessments have been completed to support new uses and label amendments. The most recent human health risk assessment for ADBAC was completed on December 19, 2013 (D413897) to assess inhalation exposures for a proposed product to be applied by fogging. The Agency's most recent ecological risk assessment for ADBAC was completed on August 2, 2006 (prepared for the RED).

1.5.1 Tolerance Information

EPA has established tolerance exemptions for indirect food uses (food-contact surfaces) for residues of some ADBAC active ingredients. The end-use concentration of all quaternary chemicals in solution is not to exceed 200 or 400 ppm of active quaternary compound. These exemptions are listed in Table 8 and are located in 40 CFR part 180.940.

Table 8 – Tolerance Exemptions under 40 CFR Part 180.940

Chemical Name	CAS No.	PC Code	Tolerance Exemption
Quaternary ammonium compounds, alkyl (C_{12}-C_{18}) benzyldimethyl, chlorides	8001-54-5	069106	When ready for use, the end-use concentration of all quaternary chemicals in the solution is not to exceed 200 ppm of active quaternary compound.
Quaternary ammonium compounds: n-alkyl (C_{12-18}) dimethyl benzyl ammonium chloride	68424-85-1	069105 069137 069141 069184	When ready for use, the end-use concentration of all quaternary chemicals in solution is not to exceed 400 ppm of active quaternary compound.
Quaternary Ammonium Compounds: n-alkyl (C_{12-14}) dimethyl ethylbenzyl ammonium chloride, average	85409-23-0		When ready for use, the end-use concentration of all quaternary chemicals in solution is not

[3] ADBAC's post-RED Generic Data Call-Ins (GDCIs) and Product Specific Data Call-Ins (PDCIs) are located at http://www.regulations.gov in docket number EPA-HQ-OPP-2006-0339.

Chemical Name	CAS No.	PC Code	Tolerance Exemption
molecular weight (in amu), 377 to 384		069154	to exceed 400 ppm of active quaternary compound.
Quaternary ammonium compounds n-alkyl (C_{12}-C_{18}) dimethyl ethylbenzyl ammonium chloride, average molecular weight (in amu) 384	8045-21-4 68956-79-6	069111 069167	When ready for use, the end-use concentration of all quaternary chemicals in the solution is not to exceed 200 ppm of active quaternary compound.

The Agency notes that not all ADBAC active ingredients have established tolerances or tolerance exemptions for residues in/on food and will evaluate the need for revisions to the existing tolerance exemptions. Table 9 lists the Agency ADBAC active ingredients with food contact product labels without a tolerance or tolerance exemption.

Table 9 – ADBAC Active Ingredients with Food Contact Product Labels without a Tolerance or Tolerance Exemption

Chemical Name	CAS No.	PC Code
Alkyl (60%C_{14}, 30%C_{16}, 5%C_{18}, 5%C_{12}) dimethyl benzyl ammonium chloride	53516-76-0	069104
Alkyl (50%C_{12}, 30%C_{14}, 17%C_{16}, 3%C_{18}) dimethyl ethylbenzyl ammonium chloride	8045-21-4	069111
Dialkyl (60% C_{14}, 30% C_{16}, 5% C_{18}, 5% C_{12}) methyl benzyl ammonium chloride	73049-75-9	069119
Benzenemethanaminium, N,N-dimethyl-N-(2-(2-(4-(1,1,3,3-tetramethylbutyl) phenoxy)ethoxy)ethyl)-, chloride	121-54-0	069122
Alkyl (60%C_{14}, 30%C_{16}, 5%C_{12}, 5%C_{18}) dimethyl ethylbenzyl ammonium chloride	68956-79-6	069167
Alkyl (67%C_{12}, 25%C_{14}, 7%C_{16}, 1%C_{18}) dimethyl benzyl ammonium chloride	68391-01-5	069175
Alkyl (67%C_{12}, 25%C_{14}, 7%C_{16}, 1%C_{8}, C_{10}, and C_{18}) dimethyl benzyl ammonium chloride	63449-41-2	128928

The following ADBAC PC Codes do not include food contact product labels and therefore do not require a tolerance or tolerance exemption: 069107, 069125, 069140, 069171, 069195 and 129012.

ADBAC has been listed as a food contact substance by the FDA under FFDCA Section 409. There is a food contact notification[4] (FCN) for ADBAC. FCNs are only effective for the manufacturer or supplier identified in the notification (see Table 10).

[4] More information about food contact notifications (FCNs) can be found at http://www.accessdata.fda.gov/scripts/fdcc/?set=fcn and http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=iaListing&page=30.

Table 10 – Summary of ADBAC Food Contact Notifications

FCN No.	Food Contact Substance	Manufacturer	Effective Date	Intended Use & Limitations/Specifications
460	Benzenemethanaminium, N,N-dimethyl-N-(2-(2-(4-(1,1,3,3,-tetramethylbutyl) phenoxy) ethoxy)-ethyl)-,chloride (CAS Reg. No. 121-54-0) also known as Benzethonium Chloride USP	Lonza, Inc.	Dec 7, 2004	As an antimicrobial agent in no-rinse hand sanitizers for food handlers. Benzethonium Chloride USP may be used at levels not to exceed 0.2 percent by weight of the finished hand sanitizer formulations.

ADBAC has also been listed as an indirect food additive under 21 CFR part 176 and 175, and as a direct food additive under 21 CFR part 172 (see Tables 11 and 12).

Table 11 – Summary of ADBAC Indirect Food Additives

CFR Section	Use	Maximum Residue Level
176.300	Slimicides used as antimicrobial agents in the manufacture of paper or paperboard that may contact food	None given
175.300	Resinous and polymeric coatings	None given
175.105	Substances for use as components of adhesives	None given

Table 12 – Summary of ADBAC Direct Food Additives

CFR Section	Use	Maximum Residue Level
172.165	Food Additives for direct addition to food for human consumption in sugar cane juice	The additive is applied to the juice in the following quantities: • n-dodecyl dimethyl benzyl (00.25-1.0 ppm) • n-dodecyl dimethyl ethylbenzyl ammonium chloride (3.4-13.5 ppm) • n-hexadecyl dimethyl benzyl ammonium chloride (1.5-6.0 ppm) • n-octadecyl dimethyl benzyl ammonium chloride (0.25-1.0 ppm) • n-tetradecyl dimethyl ammonium chloride (3.0-12.0 ppm) • n-tetradecyl dimethyl ethylbenzyl ammonium chloride (1.6-6.5)

1.6 Incidents

1.6.1 Human Health

Incidents Reported in the OPP Incident Data Center

Since the 2006 RED, 2154 individual human health incidents have been reported for ADBAC in OPP's Incident Data System (IDS) for the time period spanning from September 1, 2006 to May 2, 2016. Of these 2154 incidents, 8 involved products could not be identified and 53 involved products have since been cancelled. A summary of the remaining 2093 incidents is given in Table 13. The largest number of incidents (785) occurred when handling liquid concentrate products, followed by ready to use (RTU) spray products (316), RTU trigger sprayer products (242), and RTU wipes (240). The liquid concentrate products are used to prepare working

solutions that can be applied by a variety of methods (spray, mop, wipe or fog) thus it would be necessary to review each of the 785 incidents to determine if the exposure was caused by handling of the concentrated product during mixing/loading or application of the diluted product.

In terms of severity, most of the incidents (1962) were rated as HC (human moderate), followed by 83 rated as HB (human major), 33 rated as HD (human minor), seven rated as HA (human fatality) and eight rated as HE (severity unknown). The circumstances leading to the seven HA incidents are listed below:

- A maintenance worker at a gas station used an ADBAC/DDAC disinfectant product. Another worker there was allegedly exposed to it and developed respiratory distress and ultimately died. She had previously had chronic obstructive pulmonary disease.
- An individual ingested an ADBAC/DDAC powder product along with another non-pesticidal cleaning product in a correctional facility.
- An airline employee developed respiratory distress resulting in death. Chemical exposure to an ADBAC/DDAC product and other three cleaning products was the potential cause. No other details were provided.
- A two year old asthmatic child who used a breathing machine died after removing an ADBAC RTU household cleaning and disinfectant product from an unlocked cabinet and spilling it on toys.
- A 34 year old diabetic resident of a nursing home had a heart attack and later died at the hospital. A partially used can of ADBAC foam product was found in her room. The director of nursing indicated that this patient had previously used this product to clean her room without incident.
- A person deliberately inhaled an ADBAC foaming disinfectant product.
- A 68 year dementia patient in a nursing home ingested an ABDAC/DDAC disinfectant product that was being used to clean wheelchairs during the overnight shift.

Table 13 – Summary of ADBAC Human Health Incidents Since the RED

Type of Product (RTU = Ready to Use)	**Number of Incidents**					
	Human Fatality	**Human Major**	**Human Moderate**	**Human Minor**	**Severity Unknown**	**Total**
Liquid Concentrate	3	30	723	27	2	785
Powder or Solid	1	0	10	0	0	11
RTU Aerosol Can	1	3	52	0	0	56
RTU Foam	1	5	138	2	0	146
RTU Insecticide	0	0	4	0	0	4
RTU Solution for Pool Treatment	0	4	145	0	1	150
RTU Solution	0	5	69	0	1	75
RTU Spray	0	14	302	0	0	316
RTU Toilet Bowl Disinfectant	0	3	67	0	0	70
RTU Trigger Sprayer	1	16	222	1	2	242
RTU Wipe	0	3	220	3	2	228
Tablet	0	0	10	0	0	10
Total of Above	7	83	1962	33	8	2093

In addition to the incidents reported in individual reports discussed above, there are 15,917 incidents that were reported in quarterly aggregate incident summaries. In terms of severity, most of the aggregate incidents (15,776) were rated as HD and the remainder (141) were rated as HE.

The Agency will assess human health incidents in ADBAC's registration review risk assessment.

Epidemiology Studies and Incidents Reported in the Literature

There are reports in the literature of work-related asthma associated with exposure to cleaning agents and disinfectants and some of these reports relate to the use of the quaternary ammonium compounds (QACs). The earliest reports include a case of a laundry worker who developed asthma after using a disinfectant containing QACs (Innocenti, 1978), a pharmacist who had asthma attacks when contacting a floor cleaning solution containing QACs (Burge, 1994) and a worker who had occupational asthma caused by prolonged exposure to cleaning agents containing QACs (Berstein, 1994). Three more cases were reported in Purohit (2000) of nurses who experienced asthmas symptoms when preparing a 10% solution of disinfectant containing QAC, cleaning surgical instruments in a tray with a QAC disinfectant, and entering a room where a solution of disinfectant containing 40% QAC was kept. In a multistate report of 401 cases of pesticide related illness of health care workers (Mehler et al, 2010), QACs were involved in the most cases (151) followed by glutaraldehyde (101) and sodium hypochlorite (71). In terms of occupation, janitors and housekeepers had the most cases (95), followed by nursing/medical assistants (64) and health technicians (59).

In Gonzalez (2013) the association between disinfection with QACs and asthma in health care workers was investigated. This investigation was conducted in a cohort of 543 workers, which consisted of registered nurses (37.1%), auxiliary nurses (16.4%), cleaners (17.3%) and administrative staff (32.8%). Of the 543 workers, 335 were exposed to QACs as part of their normal workday. The nursing professionals (registered and auxiliary nurses) reported a significantly higher risk of reported physician diagnosed asthma and nasal symptoms than administrative staff. This risk was particularly marked during disinfection tasks and when exposed to QACs. Exposure to QACs increased significantly the risk of reported physician diagnosed asthma and nasal symptoms with adjusted odd ratios of 7.5 and 3.2, respectively. No significant association was found with other exposures such as latex gloves, chlorinated products/bleach or glutaraldehyde. The highest risk was associated with tasks involving dilution of disinfection products by manual mixing. An editorial on this study (Heedrick, 2014) concluded that "Initiatives are needed in particular to improve education and labeling of products and to reduce exposure to disinfectants and cleaning agents."

In response to the increasing evidence that chemicals used for environmental surface cleaning in health care can cause respiratory illnesses such as asthma, the Cleaning Disinfecting in Health Care (CDHC) Working Group was established to provide a more integrated approach to effective environmental surface cleaning and disinfection while protecting the respiratory health of health care personnel. This working group is part of the National Institutes of Safety and Health (NIOSH) National Occupational Research Agenda (NORA) and includes experts in inhalation toxicology, industrial hygiene, epidemiology, and infection control. This group recently published an article (Quinn, 2015) that discusses the potential hazards of the chemicals used for

cleaning and disinfection, including quats, and how they could be reduced by a better understanding of the efficacy of cleaning and disinfecting products and procedures. In particular, improved guidance is needed to assist health care institutions in determining if cleaning is sufficient for non-clinical public spaces and floors. Such guidance could be used to reduce the amount of disinfectant used and associated worker exposures. The article also notes that asthma symptoms or exacerbations have been associated with the use of sprays.

In contrast to the CDHC Working Group, Weber (2016) concludes that dermatitis and respiratory symptoms (e.g., asthma) as a result of chemical exposures, including low-level disinfectants, (which include ADBAC) are exceedingly rare. The authors examined the medical records for an occupational health clinic that serves the employees of the University of North (UNC) Carolina Hospital. This clinic is staffed by 2 part-time physicians, 1 full-time family nurse practitioner, and 2 full-time nurses. Over the time period studied, 2003-2012, UNC Hospital employed 69,075 full-time work years, which constituted 144 million person days of exposure. Injuries or illnesses caused by chemical exposures were uncommon. Overall, 70 of 128 chemical exposures were caused by a known germicide (i.e., antiseptic, high-level disinfectant, low-level disinfectant), including alcohol 17, quaternary ammonium compound 18, germicide (not specified) 12, glutaraldehyde 7, peracetic acid 6, hypochlorite (bleach) 5, phenol 3, and chlorhexidine 2. Other chemicals included floor strippers, cleaning agents, formaldehyde, xylene, toilet disinfectants, and miscellaneous. The authors acknowledge that unprotected exposures to high-level disinfectants may cause dermatitis and respiratory symptoms and they recommend the use of engineering controls (e.g., closed containers, adequate ventilation) and personal protective equipment (e.g., gloves) to minimize exposure to high-level disinfectants. As noted above, ADBAC is considered to be a low level disinfectant and therefore is not included in this author's recommendation for engineering controls.

The EPA plans to use all epidemiological information in ADBAC's registration review risk assessment.

1.6.2 Ecological

There are no ecological incidents in the Incident Data System (IDS) as of June 6, 2016. No ABDAC incidents have been reported with wildlife based on a search of the Ecological Incident Information System (EIIS) conducted June 9, 2016.

2 Anticipated Data Needs

Several studies were required from the assessment of ADBAC in the August 2006 Reregistration Eligibility Decision (RED). In addition to the already-required RED DCI data, the following studies as listed in Table 14 are expected to be needed for the registration review of ADBAC. Table 15 outlines the data requirements required by the post-RED GDCIs issued in December 2014. The Agency anticipates reviewing any data received in response to the post-RED DCIs as well as data required for this registration review prior to conducting the registration review risk assessments for ADBAC.

Table 14 – Antimicrobial and Conventional Studies Anticipated as Needed for the Registration Review of ADBAC

Guideline Number (GLN)	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
835.1110[1,2]	Activated Sludge Sorption Isotherm (ASSI)	TGAI	12	Ecological and Drinking Water	Antimicrobial uses: Recirculating cooling towers, air washer systems, wood preservatives, and swimming pools Conventional uses: Waste water from turf, golf courses, and ornamentals	Ecological
835.3110, 835.3220, 835.3240, or 835.3280[1,3]	WWTP Biodegradation Studies	TGAI	12	Ecological and Drinking Water		Ecological
850.3300[3,4,5]	Activated Sludge Respiration Inhibition (ASRI)	EUP, PAI, TGAI	12	Ecological and Drinking Water		Ecological
835.4100	Aerobic soil metabolism	TGAI or PAIRA	24	Ecological	Conventional uses	Ecological
Non-Guideline[6,7,8,9]	Whole sediment: chronic freshwater invertebrates (with an amphipod, for example, *Hyalella azteca*)	TGAI	24	Ecological	Antimicrobial and conventional uses	Ecological
Non-Guideline[7,8,10]	Whole sediment: chronic marine/estuarine invertebrates (with an amphipod, for example, *Leptocheirus plumulosus*)	TGAI	24	Ecological	Antimicrobial and conventional uses	Ecological
850.2100[11,12]	Avian Acute oral (with a passerine species)	TGAI	12	Ecological	Conventional uses	Ecological
850.2300[12]	Avian Reproduction	TGAI	24	Ecological	Conventional uses	Ecological
850.4100 and 850.4225[13,14]	Tiers I and II Terrestrial plant toxicity-Seedling emergence	TEP	12	Ecological	Conventional uses	Ecological
850.4150 and 850.4250[14,15]	Tiers I and II Terrestrial plant toxicity-Vegetative vigor	EUP, TGAI	12	Ecological	Conventional uses	Ecological
Non-Guideline[10,12,16]	Tier I Honey bee adult acute oral toxicity	TGAI	12	Ecological	Conventional uses	Ecological
Non-Guideline[10,12,17,18]	Tier I Honey bee larvae acute oral toxicity	TGAI	12	Ecological	Conventional uses	Ecological
Non-Guideline[10,12,18,19]	Tier I Honey bee larvae chronic oral toxicity	TGAI	12	Ecological	Conventional uses	Ecological
Non-Guideline[10,12,20]	Tier I Honey bee adult chronic oral toxicity	TGAI	12	Ecological	Conventional uses	Ecological
850.3030[12,21]	Tier I Honey bee toxicity of residues on foliage	TEP	12	Ecological	Conventional uses	Ecological

Guideline Number (GLN)	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Non-Guideline[10,12,22,23,24,25]	Tiers II and III Semi-field testing for pollinators	TEP	24	Ecological	Conventional uses	Ecological
850.3040[10,12,25,26,27,28]	Tiers II and III Field testing for pollinators	TGAI	24	Ecological	Conventional uses	Ecological
860.1340	Residue analytical method for data collection	ROC	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
860.1380	Storage stability	TEP or ROC	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
860.1480	Meat, Milk, Poultry, Eggs	TGAI	24	Dietary exposure assessment for egg wash	Antimicrobial use: Egg wash	Eggs
875.2100[29]	Turf Transferable Residue Dissipation	TEP	12	Residential Post-application	Conventional use: Turf	Dermal and Incidental Oral
875.2500[30]	Inhalation Exposure – Post Application	TEP	12	Residential Post-application	Antimicrobial use: Humidifier water	Inhalation

TGAI = Technical Grade Active Ingredient; EUP = End-Use Product; PAI = Pure Active Ingredient; PAIRA = Pure Active Ingredient, Radiolabeled; TEP = Typical End-Use Product; ROC = Residue of Concern

Footnotes

[1] If the ASSI study does not demonstrate a strong potential to sorb during activated sludge treatment, the Agency may require verification of results from the ready biodegradability study (MRID 46865601) or an appropriate WWTP biodegradability study as determined by the results of the ASRI test.

[2] EPA has published a final guideline for this study: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0003.

[3] The results of the ASRI, GLN 850.3300, will determine which of the four biodegradation tests would be expected to be required.

◦If the ASRI test EC50 is less than or equal to 20 mg/L, then either the (i) Biodegradation in Activated Sludge Study, GLN 835.3280 or (ii) Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units, GLN 835.3240, or (iii) the Porous Pot Test, GLN 835.3220 would be expected to be required. If the ASRI test EC50 is greater than 20 mg/L, then the Agency would expect to require the registrant to conduct either: (i) Ready Biodegradability (GLN 835.3110) or (ii) a) Biodegradation in Activated Sludge, or b) Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units, or c) the Porous Pot Test.

◦If the Ready Biodegradability study is conducted and passes, then no further testing would be expected to be required. If, however, the antimicrobial fails the Ready Biodegradability study, then the (i) Biodegradation in Activated Sludge, or (ii) Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units, or (iii) the Porous Pot study would be expected to be required.

[4] EPA published draft guidance under guideline 850.6800 and has since published final guidance for this study under guideline 850.3300: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0021.

[5] OECD Test Guideline 209 can also be used as guidance for this study, available online at http://www.oecd-ilibrary.org/content/book/9789264070080-en.

[6] The anticipated DCI will require conduct of the study according to ORD Study Method EPA 600/R-099-064 but with 12 replicates per treatment (4 for 28-d survival and growth and 8 for the remainder of the test) with 10 neonates per replicate.

[7] The guidance for the formulated sediment study can be found in OECD 218 Sediment-Water Chironomid Toxicity Test using Spiked Sediment.

[8] The anticipated DCI will require that a protocol be approved by the Agency prior to the initiation of the study.

[9] The guideline is partially fulfilled. Testing on one additional freshwater species is needed.
[10] The anticipated DCI will require conduct of the study according to ORD Study Method: EPA 600/R-099-020 but with 10 replicates per treatment with 20 neonates per replicate.
[11] OECD TG 233 using the "LD50- slope test" or "limit dose test" can be used instead of OCSPP 850.2100 for certain species and conditions (e.g., causes no delayed effects, causes no regurgitation). Details on the species and conditions under which TG 233 would not fulfill the data requirement are described at https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-classifying-studies-conducted-using-oecd.
[12] The study must be conducted on all conventional uses, including mosquito uses.
[13] In a Federal Register Notice dated June 27, 2012, test guidelines 850.4100 and 850.4225 were merged and harmonized into OCSPP 850.4100. See "Final Test Guidelines; OCSPP 850 Series; Notice of Availability" 77 FR 38282, June 27, 2012. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0028.
[14] Guideline studies are required to assess the impact on nontarget plants resulting from runoff and drift of the end-use products. The anticipated data are intended to provide an understanding of the relative sensitivity of a wide-range of terrestrial plants and are not intended to be specific to the actual target crop. Data are required for six species of dicots from at least four families, one species of which is soybean (Glycine max). Data are required for four species of monocots from at least two families, one species which is corn (Zea mays). At least one of either the monocot or dicot species must be a root crop.
[15] In a Federal Register Notice dated June 27, 2012, test guidelines 850.4150 and 850.4250 were merged and harmonized into OCSPP 850.4150. See "Final Test Guidelines; OCSPP 850 Series; Notice of Availability" 77 FR 38282, June 27, 2012. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0028.
[16] See the OECD 213: OECD Guidelines for the Testing of Chemicals. Honeybees, Acute Oral Toxicity Test. 213. http://www.oecd-ilibrary.org/docserver/download/9721301e.pdf?expires=1468957987&id=id&accname=guest&checksum=E4C467086668EC6F44867A9D8C5F8FA3.
[17] OECD Test Guideline 237 may be used to develop a protocol for this study (OECD. 2013 Guidelines for Testing Chemicals. Honey bee (Apis mellifera) larval toxicity test, single exposure.) See: http://www.oecd-ilibrary.org/environment/test-no-237-honey-bee-apis-mellifera-larval-toxicity-test-single-exposure_9789264203723-en.
[18] In some cases, information pertaining to acute toxicity to honey bee larvae may be obtained with the chronic honey bee larvae test thereby negating the need for separate acute and chronic larval toxicity tests.
[19] OECD has not yet finalized test guidelines for chronic studies with honey bee larvae. OECD draft guidance has is being developed, see OECD 2013b. OECD Draft Guidance Document Honey Bee (Apis mellifera) Larval Toxicity Test, Repeated Exposure. http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf.
[20] OECD has not yet finalized test guidelines for chronic studies, and efforts are underway to develop standardized guidelines for assessing the effects from chronic exposure to adult and larvae in the laboratory. Discussion of the study design elements for the 10-day adult toxicity test can be found in Appendix O of the European Food Safety Authority (EFSA) guidance document: EFSA. Guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees. EFSA Journal 2013;11(7):3295, 266 pp. doi:10.2903/j.efsa.2013.3295. Available online at: http://www.efsa.europa.eu/en/efsajournal/doc/3295.pdf.
[21] USEPA. 2012b. "Honey Bee Toxicity of Residues on Foliage." Ecological Effects Test Guidelines OCSPP 850.3030. EPA 712-C-018. Web. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0154-0017.
[22] The need for a semi-field test for pollinators (i.e., either a field-feeding test or a tunnel test) will be determined based upon lower-tiered tests and/or other lines of evidence, and the need for a refined pollinator risk assessment.
[23] Formal guidelines for semi-field tests do not yet exist; however, information that can help guide the development of either a semi-field tunnel test protocol can be found at OECD 75, see: OECD. 2007. Series on Testing and Assessment Number 75. Guidance document on the honey bee (Apis mellifera L.) brood test under semi-field conditions. Environmental Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. ENV/JM/MONO(2007)22. 31-Aug-2007. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2007)22&doclanguage=en.
[24] For field-feeding studies see: Oomen et al. 1992: Oomen, P. A. A. DeRuijter and J. Van der Steen. 1992. Method for honey bee brood feeding tests with insect growth-regulating insecticides. Bul OEPP/EPPO Bulletin 22: 613 – 616.
[25] Higher-tier colony level studies may be required pending the outcome of the screening level assessment using laboratory-based acute (single dose) and chronic (repeat dose) toxicity studies with adult and larval bees.
[26] The need for a field test for pollinators will be determined based upon lower-tiered tests and/or other lines of data and the need for a refined pollinator risk assessment.
[27] See information and guidance identified in the EPA documents, (i) USEPA. 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004; (ii) 2014 Guidance for Assessing Pesticide Risks to Bees. Office of Pesticide Programs United States Environmental Protection Agency, Health Canada Pest Management Regulatory Agency, California Department of Pesticide Regulation. June 19, 2014. http://www2.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf.

[28] USEPA. 2012c. "Field Testing for Pollinators." Ecological Effects Test Guidelines OCSPP 850.3040. EPA 712-C-017. Web. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0154-0018.

[29] In conjunction with the 2007 40 CFR Part 158 Data Requirements, HED typically requires submission of a turf transferable residue (TTR) study in order to determine exposure and risk associated with contacting treated turf. The estimated residential turf post-application exposure using default TTR values for ADBAC is not minimal in comparison to the level of concern. The calculated MOE from the 2006 RED is not greater than 10 times higher than the level of concern, with the lowest MOE = 97 compared to the LOC of 100. Future refinements of this post-application exposure for ADBAC are anticipated in order to incorporate new TTR data and to incorporate any advances in EPA risk assessment methodology. Therefore, EPA is requiring the 40 CFR TTR data to facilitate any necessary exposure assessment refinements and to further EPA's general understanding of the availability of turf transferable pesticide residues.

[30] A post application inhalation exposure study for humidifier water (MRID 47222901) was submitted after the RED, however, the LOQ of 0.026 mg/m^3 is not low enough to permit comparison to the HEC of 0.018 mg/m^3 which has a target MOE of 100. A new study needs to be conducted with an LOQ of 0.00018 mg/m^3 to allow for this comparison. In addition, the application rate of 100 ppm used in the study is less than the maximum application rate of 510 ppm allowed by the labels.

Table 15 – Antimicrobial Data Required through the December 2014 post-RED Generic Data Call-Ins (GDCIs) for ADBAC

GLN	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario	Status[12]
875.1100[1,2]	Dermal Exposure - Outdoor	TEP	24	Occupational and Residential Handler	See Footnote 1	See Footnote 1	Pending Review
875.1200[1,2]	Dermal Exposure - Indoor	TEP	12	Occupational and Residential Handler	See Footnote 1	See Footnote 1	Pending Review
875.1300[1,2]	Inhalation Exposure - Outdoor	TEP	24	Occupational and Residential Handler	See Footnote 1	See Footnote 1	Pending Review
875.1400[1,2]	Inhalation Exposure - Indoor	TEP	24	Occupational and Residential Handler	See Footnote 1	See Footnote 1	Pending Review
875.2300[3]	Indoor Surface Residue Dissipation	TEP	12	Residential Post Application	See Footnote 3	See Footnote 3	Pending Review
875.2800	Description of Human Activity	N/A	24	Occupational Post Application	All	All	Pending Review
870.3465[4]	90-day inhalation toxicity	TGAI	24	Toxicology	See Footnote 1	See Footnote 1	Waived
850.1300	Daphnid chronic toxicity test	TGAI	12	Ecological	All	All	Satisfied[13] DP Barcode: 432638
850.3020[11]	Honey bee acute contact toxicity	TGAI	12	Beneficial insects	All	All	Deficiencies / Data Gap DP Barcode: 432638
850.4225	Seedling emergence, Tier II	TEP	12	Ecological	All	Data are needed only for rice (*Oryza sativa*).	Consortia Data in Development
850.4250	Vegetative vigor, Tier II	TEP	12	Ecological	All	Data are needed only for rice (*Oryza sativa*).	Consortia Data in Development
850.4400[5]	Aquatic plant toxicity test using *Lemna spp.* Tiers I and II	TGAI	12	Aquatic plants	See Footnote 5	See Footnote 5	Deficiencies / Data Gap DP Barcode: 432638

GLN	Study Name	Test Substance	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario	Status[12]
850.4500[6,7]	Algal toxicity, Tier II	TGAI	12	Ecological	All	See Footnote 6	Consortia Data in Development
850.4550[7,8]	Algal toxicity, Tier II	TGAI	12	Ecological	All	See Footnote 8	Consortia Data in Development
Special Study[2,9]	Special Aquatic Leaching Study on Wood	TEP	12	Environmental Exposure	Wood treatment	Wood treatment	Acceptable DP Barcode: 432857
Special Study-ADBAC[10]	Dietary Residue in Food from Treating Hard Surfaces with ADBAC	TEP	12	Dietary	Hard surface products in commercial areas.	Hard surface products in commercial areas.	Acceptable DP Barcode: 435265

TGAI = Technical Grade Active Ingredient; TEP = Typical End-Use Product; N/A = Not Applicable

Footnotes
[1] Indoor hard surfaces (mop, wipe, trigger pump spray, aerosol spray, and liquid pour); Air deodorization (aerosol spray); carpets (low pressure spray); uses requiring liquid pour of formulated products; humidifier treatment; low and high pressure sprays for disinfectants (such as vehicle treatment); non-pressure treatment of wood (e.g., industrial sapstain treatments, airless sprayer of wood for existing structures); and pressure treatment of wood.
[2] A protocol must be submitted to the Agency for approval prior to the start of the study. The draft protocol was due to the Agency within 90 days of receipt of the DCI.
[3] Carpets, flooring, textiles (laundered clothing/diapers), treated wood; and musical instruments (mouthpiece/reed). Note: 100% residue transfer will be used in lieu of surface residue studies.
[4] The Hazard Science Policy Council (HASPOC) met on January 21, 2016 and determined that the ADBAC 90-day inhalation toxicity study is not required due to bridging with the DDAC 28-day inhalation toxicity study (MRID 48667903) (TXR 0057356).
[5] Data are required if algal studies show toxicity at less than 1 ppm.
[6] Data are required on 3 species: *Navicula pelliculosa, Skeletonema costatum,* and *Selenastrum capricornutum*.
[7] In a Federal Register Notice dated June 27, 2012, EPA split the Public Draft OPPTS 850.5400 test guideline into two test guidelines: OCSPP 850.4500 and OCSPP 850.4550. See "Final Test Guidelines; OCSPP 850 Series; Notice of Availability" 77 FR 38282, June 27, 2012. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0154-0028.
[8] Data are required on *Anabaena flosaquae.*
[9] Results from a study conducted according to American Wood Protection Association (AWPA) Standard E11-06 or E11-12 (Standard Method of Determining the Leachability of Wood
Preservatives) will satisfy this data requirement.
[10] A residue transfer protocol must be submitted to the Agency for approval prior to the start of the study. The draft protocol must be submitted to the Agency within 90 days of receipt of this DCI.
[11] The study must be conducted on antimicrobial wood treatment uses as well as all conventional uses, including mosquito uses.
[12] Status of the consortia, ADBAC Issues Steering Committee/Joint Venture, GDCI response.
[13] The study is classified as "Supplemental" and cannot be upgraded to "Acceptable" because of several deficiencies noted in the Data Evaluation Record (DER), DP Barcode: 432638. However, even though the study is considered "Supplemental", sufficient data are available for risk assessment. Therefore, no additional data are needed and the guideline is satisfied.

3 Human Health Risk Assessment

The Agency anticipates the need to conduct a human health risk assessment for ADBAC. The Agency anticipates requiring human health data during registration review (Table 14) and will review data required by the RED DCIs. Based on the memo from the Hazard and Science Policy Council (HASPOC) meeting on January 21st, 2016 (TXR# 0057356[5]), the acute neurotoxicity, subchronic neurotoxicity and the immunotoxicity study requirements were waived. HASPOC also agreed with the registrant working group to use the 28-day inhalation DDAC study (MRID 48667903) in lieu of conducting an ADBAC 90-day inhalation study.

3.1 Existing Toxicological Endpoints

EPA anticipates the need to revise the existing toxicological endpoints as part of this registration review. Table 16 presents the existing endpoints for ADBAC. The endpoints for dietary, dermal and incidental oral exposure were used in the EPA's human health risk assessment in support of the 2006 RED. Table 16 also includes the new ABDAC inhalation endpoint, bridged from DDAC (HASPOC memo TXR# 0057356), that was calculated as a Human Equivalent Concentration (HEC) using the LOAEC and regional dose deposition ratio (RDDR) from the 28-day inhalation toxicity study on DDAC. These data will be used in the revised risk assessment for registration review. A detailed description of the toxicity studies is provided in Appendix A.

Table 16 – Existing ADBAC Toxicological Endpoints

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE or UF, Special FQPA SF for Risk Assessment	Study and Toxicological Effects
Acute Dietary (general population; females 13+)	An acute dietary endpoint was not identified in the data base.		
Chronic Dietary	NOAEL =44 mg/kg/day	FQPA SF = 1 UF = 100 (10x inter-species extrapolation, 10x intra-species variation)	Chronic toxicity/carcinogenicity –rat MRID 41947501 LOAEL = 88 mg/kg/day, based on decreased body weight and weight gain
		Chronic RfD = 0.44 mg/kg/day	
Incidental Oral (short-term)	NOAEL = 10 mg/kg/day	FQPA SF = 1 UF = 100 (10x inter-species extrapolation, 10x intra-species variation)	Developmental Toxicity – Rat, MRID 42351501 LOAEL = 30 mg/kg/day, based on decreased body weight and food consumption

[5] The HASPOC memorandum (TXR# 0057356) titled *ADBAC: Summary of Hazard and Science Policy Council (HASPOC) Meeting of January 21, 2016: Recommendation on the Requirements for Neurotoxicity (Acute and Subchronic) Studies, Subchronic Inhalation Study and Immunotoxicity study.* can be found in the docket at www.regulations.gov, EPA-HQ-OPP-2015-0737.

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target MOE or UF, Special FQPA SF for Risk Assessment	Study and Toxicological Effects
Incidental Oral (intermediate-term)	NOAEL = 10 mg/kg/day	FQPA SF = 1 UF = 100 (10x inter-species extrapolation, 10x intra-species variation)	Developmental Toxicity – Rat, MRID 42351501 LOAEL = 30 mg/kg/day, based on decreased body weight and food consumption
Short-Term Dermal	NOAEL= 20 mg ai/kg/day (333 µg/cm^2)	FQPA SF = 1 UF = 10 (3x inter-species extrapolation, 3x intra-species variation)	21-day dermal toxicity- guinea pigs MRID 41105801 LOAEL = 40 mg ai/kg/day, based on denuded non-vascularized epidermal layer
Intermediate-Term Dermal	NOAEL = 20 mg ai/kg/day (80 µg/cm^2)	UF = 10 (3x inter-species extrapolation, 3x intra-species variation)	90-day dermal toxicity in rats MRID 41499601 20 mg ai/kg/day is the highest dose tested before irritation became significant at day 43
Long-Term Dermal (TGAI)	No appropriate endpoint identified. No systemic effects observed up to 20 mg/kg/day, highest dose of technical grade that could be tested without irritation effects.		
Inhalation (short and intermediate term)	LOAEC < 0.08 mg/m^3 (HEC = 0.018 mg/m^3)	UF = 100 (3x inter-species extrapolation, 10x intra-species variation, 3X NOAEC to LOAEC conversion)	28-day DDAC inhalation toxicity – rat, MRID 48667903 LOAEC = 0.08 mg/m^3, based on ulceration of the nasal cavity, degeneration of the olfactory epithelium, increase in mucoid production and decreased body weight/weight gain in males
Inhalation (Long term)	LOAEC < 0.08 mg/m^3 (HEC = 0.018 mg/m^3)	UF = 300 (3x inter-species extrapolation, 10x intra-species variation, 3X NOAEC to LOAEC conversion, 10X duration)	28-day DDAC inhalation toxicity – rat, MRID 48667903 LOAEC = 0.08 mg/m^3, based on ulceration of the nasal cavity, degeneration of the olfactory epithelium, increase in mucoid production and decreased body weight/weight gain in males RDDR = 0.298 (Extrathoracic Effects)

HEC = LOAEC (0.08 mg/m^3) * (6 hours/day Rat Exposure /8 hours/day Human Exposure) * RDDR (0.298)

3.2 Dietary Exposure

The last dietary exposure assessment was conducted in 2006 for the ADABC RED. EPA anticipates the need to conduct a revised dietary exposure (food and drinking water) assessment to support registration review of ADBAC since there are multiple labeled uses that could result in both direct and indirect food contact, and the dietary exposure assessment policies have been updated since 2006. The registered antimicrobial uses of ADBAC that result in dietary exposure include: (1) as a sanitizer/disinfectant in/around agricultural premises and equipment; (2) a sanitizer/disinfectant for food contact surfaces in food handling establishments/food processing plants, residential areas, and commercial areas; (3) as a materials preservative in polymers and adhesives; (4) as a slimicide in paper production; and (5) as an egg wash. The registered

antimicrobial uses of ADBAC that result in human drinking water exposure include: (1) ice machines; (2) water holding tanks; and (3) Reverse Osmosis (RO) units.

3.2.1 Food

Dietary exposure assessments will be conducted during registration review since currently registered antimicrobial uses of ADBAC may result in dietary (food) exposure. Screening-level dietary assessments were conducted in this PWP to determine anticipated data needed for the registration review of ADBAC (see Table 14). There are no conventional uses that would result in dietary (food) exposure.

A screening-level chronic (food only) dietary exposure assessment was conducted for registration review using established toxicological points of departure (PODs); an acute dietary exposure assessment was not conducted because an acute POD was not selected. The chronic population adjusted dose (cPAD) is 0.44 mg/kg/day.

A summary of the registered uses of ADBAC that are expected to result in dietary (food only) exposure is below. A residue study is available that shows the reduction of ADBAC residues from hard surfaces following a potable water rinse (PWR), or the rinsing of a hard non-porous surface with water that is potable (MRID 46870704). The results of the study indicate that after an ADBAC solution is sprayed or wiped onto a hard surface as a disinfectant, the residues are reduced by 52% from a PWR.

Additionally, a study is available that quantifies the transfer of ADBAC residues to food when food (represented by apples, bread, and bologna) contacts hard surfaces treated with ADBAC (MRID 46870703). The results of the study indicate that after treating a hard surface with ADBAC, up to 44.3% of residues may transfer to food. This represents the most conservative estimate of transferability and was generated from the bologna food samples.

Therefore, the screening-level chronic dietary exposure assessment was conducted using the maximum amount of refinement available based on chemical-specific residue estimates where appropriate (i.e., incorporating residue reductions with a PWR (as applicable) and incorporating a reduction to account for residue loss from transfer of ADBAC from hard surfaces to food).

Table 17 – Summary of Registered ADBAC Uses Expected to Result in Dietary (Food Only) Exposure

158W Use Site Category	Highest Labeled Concentration (ppm)	Representative EPA Reg. No.	PWR Adjustment[1]	Transferability Adjustment[6]
Food Handling/Storage Establishments, Premises and Equipment[3]	16,000	80346-1	Yes	Yes
Commercial, Institutional and Industrial Premises and Equipment	16,000	80346-1	Yes	Yes
	4900	70488-1	No[4]	Yes
Residential and Public Access Premises	16,000	80346-1	No[7]	No[7]
	4900	70488-1	No[4]	No[8]
Paper – Slimicides	3.3 lb ai/ton paper	10324-188	No[2]	No
Paper – Process Water[5]	246 ppm	10324-185	No[2]	No

158W Use Site Category	Highest Labeled Concentration (ppm)	Representative EPA Reg. No.	PWR Adjustment[1]	Transferability Adjustment[6]
Egg Wash	400	10324-111	No[2]	No

1. Available study results indicate that 52% of ADBAC residues will remain on surfaces following a potable water rinse after application. The highest maximum residue levels on all registered labels containing ADBAC have been corrected for this reduction when applicable. Residue value (mg) = AoS (Active on Surface = 1 mg/cm^2 * µg/g * 1g/1,000,000 µg)* Area of Treated Surface (cm^2) * Fraction Remaining on the Surface (48%)
2. Treatments not requiring a potable water rinse or for which a potable water rinse is not applicable.
3. Dietary (food only) exposure assessment for food handling/storage establishments, premises and equipment is represented by the "commercial areas" dietary exposure assessment.
4. Potable water rinse not on the label.
5. Label directions indicate 3.93 lbs of product per short ton of paper = 246 ppm ai in the slurry water (3.93 lbs * 12.5% ADBAC ÷ 0.002 lb/ton = 246 ppm).
6. Residue values adjusted for transferability data (MRID 46870703) indicating that up to 44.3% of ADBAC residues may transfer to food from hard surfaces.
7. No risk estimates of concern identified using IDREAM and the maximum concentration listed on the label; therefore additional PWR and transferability refinements were not incorporated.
8. No risk estimates of concern identified using IDREAM and the maximum concentration listed on the label; therefore additional transferability refinements were not incorporated.

Animal premises and equipment were listed as "non-food" in the use site data tables provided by the ADBAC/DDAC Issues Steering Committee/Joint Venture. The Agency relied on the information provided by the Committee in this screening assessment. The Agency considers uses on animal premises "non-food" if the labels state the following restriction:

Prior to use of this product, remove all animals {poultry} and feeds from [{premises} {areas to be treated}], animal transportation vehicles {trucks, cars}, and enclosures [{coops, crates, kennels, stables}]. Remove all litter, droppings and manure from floors, walls and surfaces of barns, pens, stalls, chutes and other surfaces of facilities and fixtures occupied or traversed by animals. Empty all troughs, racks and other feeding and watering appliances. Thoroughly clean surfaces with soap or detergent and rinse with water.

If ADBAC registrants do not currently have the above language on their labels regarding animal premises and wish this use to be considered non-food, registrants must amend their ADBAC label language through the Agency. If ADBAC registrants do not take action to make these necessary changes, registrants should anticipate that the Agency will assume that labels claiming an animal premise use are food contact uses if the use is listed as a direct or indirect food use in the Antimicrobial Use Site Index (USI) (https://www.epa.gov/pesticide-registration/antimicrobial-pesticide-use-site-index). These conservative assumptions will be made by the Agency in ADBAC's registration review risk assessment.

Although some labels allow active ingredient concentrations of up to 16,000 ppm on hard surfaces that may contact food, this concentration is greater than the currently established tolerance exemption of 200 or 400 ppm for food contact/hard surfaces in commercial areas. Therefore, for hard surfaces in commercial areas, in addition to using the label rates, the dietary exposure assessment was also conducted using the established tolerance exemption level of 400 ppm.

For dietary (food only) scenarios, a total estimated daily dietary intake (TEDDI) assessment is usually conducted to determine whether additional toxicity data (chronic/carcinogenicity studies)

are required; however, there are acceptable chronic/carcinogenicity studies available for ADBAC (see Appendix A). Therefore, an additional study is not required at this time and a TEDDI assessment has not been conducted for any dietary exposure scenarios.

Dietary Exposure Assessment – Residential Areas

Assuming the highest labeled rate (16,000 ppm)

A residential exposure assessment for hard surface products was conducted using the Indirect Dietary Residential Exposure Assessment Model (IDREAM), which is a refined Tier II model. The chronic dietary (food only) exposure and risk estimates do not exceed the level of concern (LOC) [i.e., < 100% of the PAD] for the U.S. Population or any population subgroups.

Table 18 – Chronic Exposure Assessment for Use of ADBAC in Residential Areas – IDREAM (16,000 ppm)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.0660	15
All Infants (<1 year old)	0.0487	11
Children 1-2 years old	**0.188**	**43**
Children 3-5 years old	0.159	36
Children 6-12 years old	0.101	23
Youth 13-19 years old	0.0605	14
Adults 20-49 years old	0.0543	12
Adults 50-99 years old	0.0497	11
Females 13-49 years old	0.0519	12

[1] Active on Surface (mg/cm^2) x surface area (2000 cm^2) x fraction transferred (100%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Assuming the highest labeled rate without a PWR (4,900 ppm)

Some registered labels do not require a PWR. Therefore, a residential exposure assessment for hard surface products was conducted at the highest labeled rate (4,900 ppm and 0.49% ai) without a PWR using IDREAM. The chronic dietary (food only) exposure and risk estimates do not exceed the level of concern (LOC) [i.e., < 100% of the PAD] for the U.S. Population or any population subgroups.

Table 19 – Chronic Exposure Assessment for Use of ADBAC in Residential Areas without a PWR – IDREAM (4900 ppm)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.0202	4.6
All Infants (<1 year old)	0.0149	3.4
Children 1-2 years old	**0.0577**	**13**
Children 3-5 years old	0.0487	11
Children 6-12 years old	0.0309	7.0
Youth 13-19 years old	0.0185	4.2
Adults 20-49 years old	0.0166	3.8
Adults 50-99 years old	0.0152	3.5

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
Females 13-49 years old	0.0159	3.6

[1] Active on Surface (mg/cm^2) x surface area (2000 cm^2) x fraction transferred (44.3%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Commercial Areas

Assuming the highest labeled rate, a PWR (MRID 46870704), and maximum transfer from treated hard surfaces to food (44.3%) (MRID 46870703)

In commercial areas, the chronic dietary (food only) exposure and risk estimates exceed the LOC [i.e., >100% of the PAD] for the U.S. Population, all infants < 1 year old, children 1-2 years old, children 3-5 years old, and children 6-12 years old when using the Commercial Tier 1B model for food contact (hard surfaces). This incorporates residue adjustments for the potable water rinse specified on the product labels and accounts for transfer of residues from treated hard surfaces to food as described above.

Table 20 – Chronic Exposure Assessment for Use of ADBAC in Commercial Areas Assuming Highest Labeled Rate (16000 ppm, with 48% Transfer from PWR, and 44.3% Transfer from Hard Surfaces to Food)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.1938598	44
All Infants (<1 year old)	1.7673974	400
Children 1-2 years old	1.0800762	250
Children 3-5 years old	0.7277519	170
Children 6-12 years old	0.3668183	83
Youth 13-19 years old	0.2022134	46
Adults 20-49 years old	0.1669811	38
Adults 50-99 years old	0.1675980	38
Females 13-49 years old	0.1866798	42

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm) x PWR Adjustment (48%)] x 1g/1,000,000 mg
The most highly exposed population subgroup is in bold.

Assuming the highest labeled rate without a PWR and maximum transfer from treated hard surfaces to food (44.3%) (MRID 46870703)

Some registered labels do not require a PWR. Therefore, a commercial exposure assessment for hard surface products was conducted at the highest labeled rate (4,900 ppm), assuming 44.3% transfer from hard surfaces to food, and without accounting for a PWR. In commercial areas, the chronic dietary (food only) exposure and risk estimates exceed the LOC [i.e., >100% of the PAD] for all infants (<1 year old), children 1-2 years old, children 3-5 years old, and children 6-12 years old when using the Commercial Tier 1B model for food contact (hard surfaces).

Table 21 – Chronic Exposure Assessment for Use of ADBAC in Commercial Areas Assuming Highest Labeled Rate (4900 ppm) without a PWR and 44.3% Transfer from Hard Surfaces to Food

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.124	28
All Infants (<1 year old)	**1.128**	**260**
Children 1-2 years old	0.689	160
Children 3-5 years old	0.464	110
Children 6-12 years old	0.234	53
Youth 13-19 years old	0.129	29
Adults 20-49 years old	0.107	24
Adults 50-99 years old	0.107	24
Females 13-49 years old	0.119	27

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.

Assuming the tolerance exemption of 400 ppm

In commercial areas, the chronic dietary (food only) exposure and risk estimates are not of concern [i.e., <100% of the PAD] for the U.S. population and all population subgroups, except all infants < 1 year old when using the Commercial Tier 1A model for food contact (hard surfaces). This assessment assumes no PWR but maximum transfer from hard surfaces to food (44.3%).

Table 22 – Chronic Exposure Assessment for Use of ADBAC in Commercial Areas Assuming Tolerance Exemption (400 ppm) without a PWR and 44.3% Transfer from Hard Surfaces to Food

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.0101	2.3
All Infants (<1 year old)	**0.0921**	**21**
Children 1-2 years old	0.0563	13
Children 3-5 years old	0.0379	8.6
Children 6-12 years old	0.0191	4.3
Youth 13-19 years old	0.0105	2.4
Adults 20-49 years old	0.00877	2.0
Adults 50-99 years old	0.00873	2.0
Females 13-49 years old	0.00972	2.2

[1] Exposure = Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (44.3%) ÷ BW (kg). Active on Surface (mg/cm^2) = [Residual Solution (mg/cm^2) x Active Ingredient Concentration (ppm)] x 1 g/1,000,000 mg
The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Paper Production

There are multiple end-use products for ADBAC use in paper production that may result in indirect food contact to ADBAC. The results have been presented here for ADBAC use as a slimicide during paper production and for use in paper plant process water.

Paper Mold Inhibition – Slimicide

The screening-level dietary risk assessment for ADBAC as a slimicide during paper production at a rate of 3.3 lb ai/ton of paper (EPA Reg. No. 10324-188) indicates that chronic dietary (food only) exposure and risk estimates are not of concern [i.e., <100% of the PAD] for the U.S. population and all population subgroups.

Table 23 – Chronic Exposure Assessment for Use of ADBAC as a Slimicide in Papermaking – lb ai/ton Paper

Population Subgroup	BW (kg)	Total Food Consumed (g)	DC (µg ai/g food)	EDI (µg ai/person/day)	DDD (mg/kg/day)	% cPAD
General U.S. Population	70.2	3910	0.00338	13.2	0.000188	<1
All Infants (<1 year old)	7.7	766		2.59	0.000338	<1
Children 1-2 years old	12.6	1770		5.99	0.000475	<1
Children 3-5 years old	18.7	1940		6.56	0.000351	<1
Children 6-12 years old	37.1	2460		8.32	0.000224	<1
Youth 13-19 years old	67.3	3050		10.3	0.000153	<1
Adults 20-49 years old	81.5	4110		13.9	0.000171	<1
Adults 50-99 years old	81.2	3780		12.8	0.000158	<1
Females 13-49 years old	72.9	3680		12.5	0.000171	<1

BW = Bodyweight; Mean weights from NHANES WWEIA 2003-2008
DC = Dietary concentration
EDI = Estimated daily intake = DC*Total Food Consumed
DDD = Daily dietary dose = (EDI*1 mg/1000 µg)/BW
%cPAD = % chronic Population-Adjusted Dose = (DDD/cPAD)*100%

Paper – Process Water

The screening-level dietary risk assessment for ADBAC as a mold inhibitor in paper production process water at a rate of 246 ppm (EPA Reg. No. 10324-185) indicates that chronic dietary (food only) exposure and risk estimates are not of concern [i.e., < 100% of the PAD] for the U.S. population and all population subgroups.

Table 24 – Chronic Exposure Assessment for Use of ADBAC as a Slimicide in Papermaking – Process Water

Population Subgroup	BW (kg)	Total Food Consumed (g)	DC (µg ai/g food)	EDI (µg ai/person/day)	DDD (mg/kg/day)	% cPAD
General U.S. Population	70.2	3910	0.4595	1797	0.0256	5.8
All Infants (<1 year old)	7.7	766		352	0.0457	10
Children 1-2 years old	**12.6**	**1770**		**813**	**0.0645**	**15**
Children 3-5 years old	18.7	1940		891	0.0477	11
Children 6-12 years old	37.1	2460		1130	0.0305	7.0
Youth 13-19 years old	67.3	3050		1401	0.0208	4.7
Adults 20-49 years old	81.5	4110		1889	0.0232	5.3
Adults 50-99 years old	81.2	3780		1737	0.0214	4.9
Females 13-49 years old	72.9	3680		1691	0.0232	5.3

BW = Bodyweight; Mean weights from NHANES WWEIA 2003-2008
DC = Dietary concentration
EDI = Estimated daily intake = DC*Total Food Consumed
DDD = Daily dietary dose = (EDI*1 mg/1000 µg)/BW
%cPAD = % chronic Population-Adjusted Dose = (DDD/cPAD)*100%

Dietary Exposure Assessment – Egg Wash

There are multiple products containing ADBAC that allow use as an egg-shell sanitizer. Therefore, a screening-level chronic dietary (food-only) exposure analysis was completed to evaluate the direct treatment of egg shells using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16. This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA).

For a chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food-commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

The maximum allowed residue found on all registered ADBAC labels based on information provided by the ADBAC/DDAC Issues Steering Committee/Joint Venture was 400 ppm. Therefore, a residue value of 400 ppm was entered into DEEM for all egg commodities. The screening-level dietary risk assessment indicates that chronic dietary (food only) exposure and risk estimates are of concern [i.e., >100% of the PAD] for children 1-2 years old; the U.S. population and all other population subgroups are not of concern.

Table 25 – Chronic Exposure Assessment for Use of ADBAC as an Egg Wash (400 ppm)

Population Group	Exposure[1]	Risk Estimates
	Exposure (Dose) (mg/kg/day)	% cPAD
General U.S. Population	0.161	37
All Infants (<1 year old)	0.123	28
Children 1-2 years old	**0.507**	**120**
Children 3-5 years old	0.380	86
Children 6-12 years old	0.215	49
Youth 13-19 years old	0.114	26
Adults 20-49 years old	0.133	30
Adults 50-99 years old	0.138	31
Females 13-49 years old	0.117	27

[1] Active on Surface (mg/cm^2) x surface area (4000 cm^2) x fraction transferred (100%) ÷ BW (kg)
The most highly exposed population subgroup is in bold.

Dietary Exposure Assessment – Conclusions

The chronic dietary exposure assessment for the registered uses of ADBAC at the maximum labeled rates are of concern, even when incorporating available data on transferability of residues from treated hard surfaces to food and data on reduction of residues following a potable water rinse, where applicable. However, the Agency does not anticipate the need to call in any additional data for indirect food uses at this time since chemical specific data representing a PWR as well as migration data have previously been submitted/reviewed and incorporated into

the assessments herein. During the registration review process, additional refinements to the dietary exposure assessment may be performed to further refine estimated exposures from the indirect food uses of ADBAC. The Agency notes that the product use rates assessed for commercial areas (16000 ppm with a PWR and 4900 ppm without a PWR) are both well-above the established tolerance exemption level for ADBAC.

Because the use on eggs is considered a direct food use and results in risks of concern, magnitude of the residue data on eggs are required (OCSPP Guideline 860.1480). The use on eggs will be reassessed when data are submitted. Supporting storage stability data (OCSPP Guideline 860.1380) as well as a residue analytical method for data collection (OCSPP Guideline 860.1340) are also required. These anticipated data needs are listed in Section 2, Table 14.

3.2.2 Drinking Water

A drinking water assessment was not conducted in 2006 as part of the RED for ADBAC. The Agency determined at that time that the registered antimicrobial uses of ADBAC were not expected to significantly impact surface or ground water resources. The following uses of ADBAC may result in drinking water exposure from surface water downstream of Waste Water Treatment Plants (WWTPs): cooling tower water systems; air washers; pulp and paper mills; down-the-drain exposure from hospital and swimming pool uses; wood preservative uses; and turf, golf course, and ornamental uses. In the absence of environmental fate data on sorption to activated sludge and toxicity to WWTP microorganisms, the Agency assumes that these uses can result in continuous exposure to surface water at low concentrations even though the primary route of dissipation of ADBAC in the aquatic environment is sorption to sediment (bottom and suspended) (MRID 40835604 and 41105501). If WWTP environmental fate and effects data required for registration review demonstrate high removal by sorption to sludge and a relatively low toxicity to WWTP microorganisms, the Agency does not anticipate conducting a drinking water risk assessment from ADBAC in surface water downstream of WWTPs. However, in the absence of the WWTP studies or if the submitted data do not demonstrate high removal by sorption to sludge and a relatively low toxicity to WTTP microorganisms, the Agency will conduct a drinking water assessment.

Other potential sources of human exposure to drinking water are from ADBAC added to the interior of ice machines and the interior of water holding tanks, as well as application to Reverse Osmosis units in water holding tanks. A dietary risk assessment will include drinking water from these other potential sources and food uses.

3.3 Occupational and Residential Exposures

The Agency anticipates the need to revise the occupational and residential assessments conducted for the antimicrobial and conventional uses in support of the 2006 RED since the Margins of Exposures (MOEs) were calculated using toxicological point of departures (PODs) and exposure data that have since been updated. In particular, it will be necessary to reassess the inhalation exposures using the HEC of 0.018 mg/m^3 from the DDAC inhalation toxicity study (see Table 16) that was submitted after the RED. In addition, ADBAC's RED required label changes to mitigate occupational and residential exposures include the following:

- Add re-entry interval (REI) of 2 hours to all labels listing hatcheries fogging as a use.
- Add REI of 2 hours as well as a minimum of 4 air exchanges (ACH) per hour in the facility to all labels listing food processing plants fogging as a use.
- Add restriction that swimming pool use products must not be applied when swimmers are in the immediate vicinity. Add REI of 15 minutes to all labels listing swimming pools as a use.

The Agency anticipates that some mitigation measures may change due to changes in ADBAC's toxicological endpoints. The uses of ADBAC that may result in occupational and residential handler and post-application exposures are presented in Table 26, 27, 28 and 29. These tables include exposure scenarios for both the antimicrobial and conventional uses of ADBAC.

3.3.1 Occupational Handler Exposure

EPA anticipates the need to revise the occupational handler assessment conducted in support of the 2006 RED. In response to the need for indoor dermal and inhalation exposure data for antimicrobial chemicals, the Antimicrobial Exposure Assessment Task Force II (AEATF II) has completed exposure studies for several scenarios including liquid pour, solid pour, trigger spray and wipe, aerosol can application, mopping and pressure treatment wood preservation. These studies have been reviewed by the Agency in conjunction with the Human Studies Review Board and have been found to be ethically and scientifically acceptable for use in risk assessment. The data from these studies will be used to assess occupational and residential handler exposures for antimicrobial chemicals. In addition, two sapstain worker exposure studies (MRID 45524304 and 47618301) sponsored by the Sapstain Industry Group (SIG) were previously submitted to EPA and will be used to assess occupational handler exposures during sapstain treatment. In addition, the inhalation component of the SIG study was conducted for comparison to the inhalation toxicity endpoint that existed at the time of the study (the oral NOAEL of 8 mg/kg/day) and thus the LOD of 5.8 ug/m^3 that was used may not be low enough to allow assessment of exposures to the revised HEC of 0.018 mg/m^3 (18 ug/m^3) that is based on the inhalation toxicity study.

To assess occupational handler exposures for the conventional uses, the Agency will use the unit exposure data listed in the Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (US EPA, 2015). This table includes exposure data from the Agricultural Handler Exposure Task Force (AHETF) and the Outdoor Residential Exposure Task Force (ORETF).

It should be noted that data from the AHETF, ORETF, AEATF II and SIG are subject to data compensation. The occupational handler scenarios to be assessed are presented in Table 26.

Table 26 – Occupational Handler Exposure Scenarios for ADBAC

Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Open pour for industrial process and water systems treatment	Dermal, Inhalation	Short and Intermediate Term

Scenario	Exposure Routes	Duration
Wood Preservation – Pressure Treatment	Dermal, Inhalation	Short, Intermediate, and Long Term
Wood Preservation – Spray or dip treatment for sapstain control	Dermal, Inhalation	Short, Intermediate, and Long Term
Wood Preservation – Spray treatment of existing shingle and shake structures	Dermal, Inhalation	Short and Intermediate Term
Hard surface disinfection using low pressure handwands, high pressure handwands, aerosol cans, trigger sprayers, mops and wipes.	Dermal, Inhalation	Short, Intermediate, and Long Term
Hard surface disinfection using handheld foggers or misters	Dermal, Inhalation	Short and Intermediate Term
Conventional Uses		
Mosquito Control in Ornamental Ponds and Fountains – Open pour liquid	Dermal, Inhalation	Short and Intermediate Term
Turf, Sod-farm - Mix/load liquids, mix/load wettable powder, ground boom application	Dermal, Inhalation	Short and Intermediate Term
Turf, Golf Course, Residential, and Commercial – Mix/load liquids, mix/load wettable powder, ground boom application, mechanically pressurized handwand application	Dermal, Inhalation	Short and Intermediate Term
Ornamental Herbaceous Plants, Shrubs, and Trees - Mix/load liquids, mix/load wettable powder, mechanically pressurized handwand application, manually pressurized handwand application, airblast sprayer application	Dermal, Inhalation	Short and Intermediate Term
Seedlings after Planting– Mix/load liquids, mix/load wettable powder, ground boom application, mechanically pressurized handwand application, manually pressurized handwand application	Dermal, Inhalation	Short and Intermediate Term
Carnations - Mix/load liquids, mix load wettable powder ground boom application, mechanically pressurized handwand application, manually pressurized handwand application	Dermal, Inhalation	Short and Intermediate Term
Seedlings Before Planting, Cuttings and Bulbs – Dip Treatment	Dermal, Inhalation	Short and Intermediate Term

3.3.2 Occupational Post Application Exposures

EPA anticipates the need to revise the occupational post application exposure assessment conducted in support of the 2006 RED. No additional data is needed to assess post application exposures for the antimicrobial uses of ADBAC. To assess post application exposures for the conventional uses, a turf transferable residue (TTR) study (Guideline #875.2100) is anticipated to be needed. The occupational post-application exposure scenarios to be assessed are presented in Table 27.

Table 27 – Occupational Post-Application Exposure Scenarios for ADBAC

Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Post Application Exposure to fogging treatments	Inhalation	Short, Intermediate, and Long Term

Conventional Uses		
Post Application to Turf	Dermal	Short and Intermediate Term
Post Application to Ornamentals	Dermal	Short and Intermediate Term

3.3.3 Residential Handler Exposures

EPA anticipates the need to revise the residential handler assessment conducted in support of the 2006 RED. To assess residential handler exposures for the antimicrobial uses of ADBAC, the Agency will use the data from AEATF as discussed above for occupational handlers. To assess residential handler exposures for the conventional uses of ADBAC, the Agency will use the unit exposures from the Standard Operating Procedures for Residential Pesticide Exposure Assessment (US EPA, 2012). The residential handler exposure scenarios that will be evaluated are listed in Table 28.

Table 28 – Residential Handler Exposure Scenarios for ADBAC

Scenario	Exposure Routes	Duration
Antimicrobial Uses		
Hard surface disinfection using aerosol cans, trigger sprayers, mops and wipes	Dermal, Inhalation	Short, Intermediate, and Long Term
Soft surface sanitization of carpets using low pressure sprayers	Dermal, Inhalation	Short Term
Air freshener treatments using aerosol can	Inhalation	Short, Intermediate, and Long Term
Open pour for pool and spa treatment	Dermal, Inhalation	Short Term
Wood Preservation – Spray and brush treatment of existing shingle and shake structures	Dermal, Inhalation	Short Term
Conventional Uses		
Residential turf and ornamental plants and shrubs - Mix /Load /Apply liquid using a manually pressurized handwand, hose end sprayer, or backpack sprayer	Dermal, Inhalation	Short Term
Residential turf and ornamental plants and shrubs - Mix /Load /Apply wettable powder using a manually pressurized handwand, hose end sprayer, or backpack sprayer	Dermal, Inhalation	Short Term
Cutting and bulbs – Dip Treatment	Dermal, Inhalation	Short Term

3.3.4 Residential Post-Application Exposures

EPA anticipates the need to revise the residential post-application assessment conducted in support of the 2006 RED. To assess post application exposures for the antimicrobial uses, a post application inhalation exposure study (Guideline #875.2500) is anticipated to be needed. This

study is needed to assess inhalation exposures resulting from the use of ADBAC in humidifier water. A post application inhalation exposure study (MRID 47222901) for the humidifier use was submitted after the RED, however, the LOQ of 0.026 mg/m^3 is not low enough to permit comparison to the HEC of 0.018 mg/m^3 which has a target MOE of 100. In addition, the application rate of 100 ppm used in the study is less than the maximum application rate of 510 ppm allowed by the labels. A new study needs to be conducted with an LOQ of 0.00018 mg/m^3 to allow for comparison to the HEC and this study should be done at an application rate of 510 ppm. To assess post application exposures for the conventional uses, a turf transferable residue (TTR) study (Guideline #875.2100) is anticipated to be needed. The residential post-application exposure scenarios to be assessed are presented in Table 29.

Table 29 – Residential Post-Application Exposure Scenarios for ADBAC

Exposed Population	Exposure Scenario	Exposure Routes	Duration
Antimicrobial Uses			
Children	Mouthing treated laundry	Incidental Oral	Short and Intermediate Term
Children	Playing on decking and playground equipment	Dermal, Incidental Oral	Short and Intermediate Term
Children	Playing on treated floors and carpets	Dermal, Incidental Oral	Short and Intermediate Term
Children and Adults	Humidifier Treatment	Inhalation	Short and Intermediate Term
Children and Adults	Air freshener treatments	Inhalation	Short and Intermediate Term
Children and Adults	Swimming in treated pools	Dermal, Incidental Oral	Short and Intermediate Term
Children and Adults	Wearing treated laundry	Dermal	Short and Intermediate Term
Conventional Uses			
Children	Playing on Treated Turf	Incidental Oral	Short Term
Children and Adults	Residential Turf	Dermal	Short Term
Adults	Ornamentals	Dermal	Short Term

3.4 Aggregate and Cumulative Exposure

3.4.1 Aggregate Exposures

EPA anticipates the need to revise the aggregate assessment conducted in support of the 2006 RED. Aggregate exposures will need to be assessed upon reevaluation of the aggregate assessment and toxicological endpoints, combined with the human health exposure assessments expected as a part of this registration review case. This assessment will include dietary (food and water) exposures and residential exposures.

3.4.2 Cumulative Exposures

In 2015, EPA's Office of Pesticide Programs released a guidance document entitled, Pesticide Cumulative Risk Assessment: Framework for Screening Analysis. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. In May 2016, a final version of this guidance document was released (U.S. EPA, 2016) stating that non-specific toxic effects, such as irritation, unless tied to a mode of action (MOA)/adverse outcome pathway (AOP) or testable hypothesis related to a potential MOA/AOP, would not support a candidate common mechanism group (CMG). This framework supplements the existing guidance documents for establishing common mechanism groups[6] and conducting cumulative risk assessments.[7]

The Agency has utilized this framework for ADBAC and notes that irritation endpoints are not considered for cumulative assessments for ADBAC and any other substances. Also, ADBAC does not appear to produce a toxic metabolite produced by other substances. The Agency notes that the individual exposure scenarios in ADBAC assessments are developed by summing the total percent of ADBAC active ingredients on a product's label. For the purposes of this registration review, the Agency is not conducting a cumulative assessment. For information regarding the Agency's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see http://www.epa.gov/pesticides/cumulative/.

4 Environmental Risk Assessment

The Agency has not previously conducted a risk assessment that supports a complete endangered species determination for ADBAC. At this time the Agency anticipates that, as part of registration review, an ecological risk assessment will be needed for ADBAC based on the uses of ADBAC in cooling tower water systems; air washers; pulp and paper mills; down-the-drain exposure from hospital and swimming pool uses; wood preservative uses; and turf, golf course, and ornamental uses. The ecological risk assessment planned during registration review will allow the Agency to determine potential acute and chronic risks to aquatic organisms exposed to residues of ADBAC that are transported from treatment sites into the aquatic environment.

Such sites include: cooling tower water systems; air washers; pulp and paper mills; down-the-drain exposure from hospital and swimming pool and spa uses; wood preservatives; and turf, golf course, and ornamental uses. There is potential for acute exposure to aquatic organisms in the water column because of the high solubility of ADBAC in water (Table 4). However, bioconcentration in aquatic organisms is not expected despite the high log K_{ow} of 3.91 (>3) because ADBAC is highly soluble in water and, being a positively-charged compound, is tightly sorbed to soil and sediment, which are typically negatively-charged. Chronic exposure to sediment-dwelling organisms from both antimicrobial and conventional uses is expected to occur

[6] Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (U.S. EPA, 1999)
[7] Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity (U.S. EPA, 2002)

based on the sorption potential from the positively-charged parent compound. Potential acute and chronic risks to terrestrial as well as aquatic organisms will be assessed for the conventional uses (*e.g*. applications to turf and golf courses) of ADBAC.

The risk assessment also will allow the Agency to determine whether each use of the ADBAC has 'no effect' or 'may affect' federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use 'may affect' a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services), as appropriate.

4.1 Environmental Fate Assessment

ADBAC is completely soluble in water, and based on its low vapor pressure and Henry's Law value (Table 4), is not expected to partition from soil and water into air. ADBAC is stable to hydrolysis at pH values of 5, 7, and 9 (MRID 40835602), with half-lives ranging from 150 to 379 days, and stable to photodegradation in pH 7 buffered aqueous solutions, but degraded in water in the presence of a photosensitizer with a half-life of 7 days (MRID 40835603).

Test data indicate that ADBAC would be expected to be amenable to both sorption and biodegradation. The high log Kow of 3.91 (Table 4) indicates that ADBAC is relatively hydrophobic, partitioning more to octanol than to water. Log Koc values of greater than 6 (MRIDs 40835605 and 42414801) indicate that ADBAC would be expected to be immobile due to strong sorption to soil and sediment. In aqueous media offering the potential for both sorption and biodegradation, there is conflicting information about which of these processes would be expected to predominate. Based on results of aerobic and anaerobic aquatic metabolism studies (MRID 40835604, 41105501, 42415101), ADBAC was indicated to be stable to microbial degradation under aerobic conditions and anaerobic conditions in water and sediment, indicating that sorption would predominate. In contrast, in a ready biodegradability study ADBAC met key criteria that indicate it is readily biodegradable (MRID 46865601), with 95.5% of ADBAC biodegraded after 28 days, indicating that biodegradation would predominate.

A possible explanation of these apparently conflicting indications about whether sorption or biodegradation of ADBAC would predominate is the difference between the test media used in the ready biodegradability study and the aquatic metabolism studies. The stability of ADBAC in the aerobic and anaerobic aquatic metabolism studies can be attributed to strong sorption of ADBAC to sediment present in a test medium that allows for both sorption and microbial degradation. In contrast, the finding of ready biodegradability of ADBAC in the ready biodegradability study can be attributed to the influence of biodegradation which occurred in a medium in which microorganisms present are acclimated to experimental conditions that are typical of wastewater treatment plants. Consequently, these conditions would be expected to favor biodegradation over sorption of ADBAC.

There is uncertainty about whether sorption or biodegradation of ADBAC would predominate during wastewater treatment. In the absence of data on the extent for ADBAC to sorb to sludge biomass during wastewater treatment, data from an Activated Sludge Sorption Isotherm (ASSI) study (GLN 835.1110) are needed. If the results from this study do not indicate a high potential

for ADBAC to sorb to sludge biomass, the Agency may require additional information on the ready biodegradability study (MRID 46865601) submitted to the Agency so it can be upgraded to an acceptable status. If results from the ASRI study, however, indicate high toxicity to activated sludge microorganisms (EC_{50} less than or equal to 20 mg/L), the Agency may require a wastewater treatment plant biodegradation simulation test rather than a ready biodegradability test.

Data relevant to aerobic soil metabolism have not been submitted and are anticipated to be required for conventional uses. Sorption to soil, sediment, and sludge is expected to be the primary route of dissipation from water based on the fact that this is a quaternary ammonium compound with a positive electrical charge that will sorb to negatively-charged (*e.g.*, clay) particles. In soil and sediment, ADBAC is expected to be immobile based on the Freundlich K_{ads} values of 5,123 – 32,429 L/kg and K_{oc} values of 640,389 – 6,171,657 L/kg_{oc}[8] (MRID 40835605 and 42414801). Because of its strong sorption to soils, ADBAC is not expected to leach to ground water or be present in dissolved form in runoff water discharged to surface water. ADBAC, however, is expected to be associated with the eroded sediment that is transported during runoff. There are no major degradates of ADBAC based on its stability to microbial metabolism in the environment.

4.1.1 Leaching (Treated Wood)

Based on similar chemical and physical properties of ADBAC and DDAC, bridging of wood leaching data between these two active ingredients is appropriate. A study done on DDAC (MRID 49812403) demonstrated leaching rates for DDAC from treated blocks were essentially proportional to the treatment rate of the wood. At the end of a 14-day period the total amount of DDAC leached ranged from 2.6-8.2%, with maximum leach rates of 1,219-13,330 ug/cm^2/day at 0.8-3.2 % w/w.

4.1.2 Wastewater Treatment Plants (WWTPs)

If the Activated Sludge Sorption Isotherm (ASSI) study does not demonstrate a strong potential to sorb during activated sludge treatment, the Agency may require verification of results from the ready biodegradability study (MRID 46865601) or an appropriate WWTP biodegradability study as determined by the results of the Activated Sludge Respiration Inhibitor (ASRI) test. The Agency received a ready biodegradability study (MRID 46865601) that was classified as upgradeable rather than acceptable and the results contradicted the persistence of ADBAC demonstrated in the aerobic aquatic metabolism study (MRID 40835604).

4.1.3 Water Quality

ADBAC is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[9]. In addition, no Total Maximum Daily Loads (TMDL)

[8] Based on the Food and Agriculture Organization of the United Nations (FAO) soil classification of mobility, http://www.fao.org/docrep/003/x2570e/x2570e06.htm
[9] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

have been developed for ADBAC[10]. More information on impaired water bodies and TMDLs can be found at EPA's website[11].

4.2 Conceptual Models for Environmental Exposure Pathways

Based on the summary of registered uses of ADBAC presented in Table 6, physical/chemical properties and environmental fate data presented in Table 4 and Appendix B, the Agency has developed conceptual model diagrams for exposure of ecological organisms to ADBAC. Under environmental conditions where ADBAC is likely to be released, ADBAC is not likely to hydrolyze (MRID 40835602). ADBAC is not expected to photolyze in water without a sensitizer (*e.g.*, acetone) present (MRID 40835603).

Chemicals that are released down-the-drain can typically take from a few to several hours to reach wastewater treatment plant intakes following their discharge down-the-drain and from several hours to roughly a day following their discharge to subsequently be discharged from wastewater treatment plants to surface water. Since ADBAC is stable to chemical degradation (hydrolysis and photodegradation), ADBAC is expected to enter wastewater treatment plants as a result of down-the-drain discharges of ADBAC. Sorption to sludge is expected to be the main pathway for removal of ADBAC entering WWTPs but data on this pathway have not been submitted. Because of ADBAC's expected stability in the aquatic environment, aquatic organisms in surface water downstream of both direct and indirect sources of ADBAC would be expected to be exposed to ADBAC and not its degradation products.

The Agency has created conceptual models for potential routes of environmental exposure which are included in "Conceptual Models for Environmental Exposure Pathways of Antimicrobial Pesticides", found in the docket at www.regulations.gov, EPA-HQ-OPP-2014-0638-0002.

Use sites and corresponding figures of conceptual model diagrams are as follows:

- Cooling towers and air washer systems (slides 13 and 14)
- Pulp and paper mill use (slide 26)
- Swimming pool and spa use (slides 27 and 28)
- Wood preservative industrial use (slide 29) or professional/amateur in-service use (slides 30 and 31)

For conventional uses (*e.g.* applications to turf and golf courses), ecological receptors that may potentially be exposed to ADBAC include terrestrial and semiaquatic wildlife (*i.e.*, mammals, birds, amphibians and reptiles), terrestrial and semi-aquatic plants, and terrestrial soil and aquatic sediment invertebrates. Additionally, aquatic organisms (*i.e.*, freshwater and estuarine/marine fish and invertebrates, amphibians, and aquatic plants) are potential receptors in adjacent water bodies through the off-site transport of ADBAC from the application site through erosion and

[10] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[11] http://www.epa.gov/owow/tmdl/

spray drift (commercial turf and golf courses). Based on ADBAC's sorption properties, it is not expected that off-site transport via runoff water discharged to surface water will be of concern.

4.3 Ecological Effects Assessment

4.3.1 Ecotoxicity Endpoints

Acute and chronic toxicity data from registrant-submitted studies (850 OCSPP Harmonized Test Guidelines[12]) are used to evaluate the potential effects of the ADBACs to aquatic and terrestrial nontarget organisms. Available ecotoxicity endpoints, data requirements, and data gaps for the ADBACs are presented in Appendix C. OPP uses the most sensitive of these endpoints for assessing risks to each receptor group. The endpoints currently available for risk assessment are listed in Table 30.

On an acute exposure basis, ADBAC is highly toxic to freshwater and marine/estuarine fish and freshwater invertebrates. Freshwater invertebrates are especially sensitive to ABDAC on an acute exposure basis, as the acute toxicity classification for ABDAC is very highly toxic (Appendix C). On a chronic exposure basis, freshwater invertebrates are also very sensitive to ABDAC (Appendix C). Chronic data for marine/estuarine invertebrates are expected to be needed, as well as data for aquatic and terrestrial plants (Table 14). These data are needed to support the conventional uses of ABDAC which can be used outdoors. ABDAC is moderately toxic to birds on an acute oral exposure basis. Some data on toxicity to birds have not been submitted, and these data are needed to support the conventional uses (850.2100 with a passerine species and 850.2300). Also, due to the physio-chemical properties of ABDAC, sediment toxicity data are needed. Finally, no toxicity data have been submitted for beneficial insects, and these data are needed to understand the potential risk to beneficial insects from the conventional uses.

Table 30 – Existing Ecotoxicity Endpoints

Receptor Group	Test Material	Exposure Scenario	Toxicity Endpoint	Reference
Freshwater fish	TGAI	Acute	LC_{50} = 280 µg ai/L	43740103
		Chronic	NOAEC = 32.2 µg ai/L	42302102
Freshwater invertebrates	TGAI	Acute	EC_{50} = 5.9 µg ai/L	41947203
		Chronic	NOAEC = 4.15 µg ai/L	42302101
Estuarine/marine fish	TGAI	Acute	LC_{50} = 310 µg ai/L	Dobbs et al. 1995
Estuarine/marine invertebrates	TGAI	Acute	EC_{50} = 55 µg ai/L	42479503
Freshwater benthic invertebrates[1]	TGAI	Chronic	NOAEC = 520 mg ai/L sediment	43731101
Estuarine/marine benthic invertebrates	TGAI	Chronic	Data gap	--
Aquatic plants (vascular)	TGAI	Aquatic Plants Toxicity (Tiers 1+II)	Data gap	--

[12] https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances

Aquatic plants (algal)	TGAI	Algal toxicity (Tiers 1+II)	Data gap	--
Terrestrial Plants	TEP	Seedling Emergence (Tiers 1+II)	Data gap	--
		Vegetative Vigor (Tiers 1+II)	Data gap	--
Birds	TGAI	Acute	LD_{50} = 136 mg ai/kg bw	42885901
		Dietary	LC_{50} =2565 ppm	00119707
Beneficial insects	TGAI	Honey bee adult acute oral	Data gap	--
Beneficial insects	TGAI	Honey bee adult acute contact	Data gap	--
Beneficial insects	TGAI	Honey bee adult chronic oral	Data gap	--
Beneficial insects	TGAI	Honey bee larvae acute oral	Data gap	--
Beneficial insects	TGAI	Honey bee larval chronic larval	Data gap	--
Beneficial insects	TEP	Honey bee toxicity of residues on foliage	Data gap	--
Beneficial insects	TEP	Semi-field testing for pollinators	Data gap	--
Beneficial insects	TEP	Field testing for pollinators	Data gap	--

[1] Data are partially satisfied. One additional freshwater species is needed.

4.3.2 Open Literature

The ECOTOXicology (ECOTOX) is a source for locating single chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The database will be searched when the risk assessment is conducted. Any acute or chronic endpoints more sensitive than what is currently available may be used in the risk assessment. Other relevant information also may be used to characterize risks. ECOTOX was created and is maintained by the U.S. EPA, Office of Research and Development (ORD), and the National Health and Environmental Effects Research Laboratory's (NHEERL's) Mid-Continent Ecology Division (MED).
https://cfpub.epa.gov/ecotox/

4.4 Exposure Analysis Plan

4.4.1 Aquatic and Terrestrial Wildlife Exposure Estimates

For antimicrobial uses, if the results of sorption data on ADBAC do not eliminate potential concerns regarding potential exposures of aquatic organisms to ADBAC, available OPP models will be used to determine estimated environmental concentrations (EECs) in the aquatic environment. Uses of ADBAC expecting to result in down-the-drain releases include industrial uses and non-industrial uses, such as residential, commercial, and institutional uses. For those non-industrial uses of ADBAC, such as swimming pools and spas that are expected to result in releases down-the-drain to domestic WWTPs, EPA anticipates the need to use the Down-the-Drain module of Exposure and Fate Assessment Screening Tool (E-FAST), https://www.epa.gov/tsca-screening-tools/exposure-fate-assessment-screening-tool-e-fast-version-20-computer-based, to estimate the number of days of exceedance of concentrations of concern for aquatic organisms downstream of domestic WWTPs. For those industrial uses of ADBAC, such as cooling water systems, air washer systems, and pulp and paper mills that are expected to result in releases down-the-drain to industrial WWTPs, EPA anticipates the need to use the General Population and Ecological Exposure from Industrial Releases module of E-FAST to estimate the number of days of exceedance of concentrations of concern for aquatic organisms downstream of industrial WWTPs. Concentrations of concern for aquatic organisms are based on toxicity endpoints selected to represent each key receptor group, such as freshwater fish, freshwater invertebrates, aquatic plants, estuarine/marine fish, and estuarine/marine invertebrates.

For conventional uses, measures of exposure are based on aquatic and terrestrial models that predict EECs of ADBAC using maximum labeled application rates and application methods that have the greatest potential for off-site transport of the chemical. The models used to predict aquatic EECs are the Pesticide Root Zone Model coupled with the Variable Volume Water Model (PRZM/VVWM). For exposure to sediment dwelling organisms, predicted pore water EECs are generated using PRZM/VVWM.PRZM (v 5.0+, July 2014) and VVWM (v 1.0, June 2014) are simulation models coupled with the graphical user interface, Pesticide in Water Calculator (v 1.52, May 2016) to generate daily exposures and 1-in-10-year EECs of ADBAC that may occur in surface water bodies adjacent to application sites receiving ADBAC through erosion and spray drift. PRZM simulates pesticide application, movement and transformation on an agricultural field and the resultant pesticide loadings to a receiving water body via runoff, erosion, and spray drift. VVWM simulates the fate of the pesticide and resulting concentrations in the water body. The standard watershed geometry used for ecological pesticide assessments assumes application to a 10-hectare agricultural field that drains into an adjacent 1-hectare water body that is 2 meters deep (20,000 m3 volume) with no outlet. The composite model PRZM/VVWM is used to estimate exposure of aquatic organisms to ADBAC at a location that is expected to be more vulnerable than most locations where a specific crop is crown. Therefore, the resulting exposure estimates are expected to be protective of aquatic wildlife in most locations. Measures of exposure for aquatic species include the 1-in-10-year peak and 1-in-10-year rolling mean concentrations. The 1-in-10-year peak is used for estimating acute exposures of direct effects to aquatic organisms. The 1-in-10-year 60-day mean is used for assessing

chronic exposure to fish and aquatic-phase amphibians. The 1-in-10-year 21-day mean is used for assessing aquatic invertebrate chronic exposure.

KABAM v.1.0 is used to estimate potential bioaccumulation of ADBAC in freshwater aquatic food webs and subsequent risks to mammals and birds via consumption of contaminated aquatic prey. At this time, no tool is available in EFED to quantify the bioaccumulation potential of ADBAC in terrestrial food webs.

Exposure estimates for terrestrial animals assumed to be in the target area or in an area exposed to spray drift are derived using the T-REX model (version 1.5.2, June 2013). This model incorporates the Kenaga nomograph, as modified by Fletcher et al. (1994), which is based on a large set of actual field residue data. The upper limit values from the nomograph represent high end residue values from actual field measurements (Hoerger and Kenaga, 1972). The Fletcher et al. (1994) modifications to the Kenaga nomograph are based on measured field residues from 249 published research papers, including information on 118 species of plants, 121 pesticides, and 17 chemical classes. Given that no suitable data on interception and subsequent dissipation from foliar surfaces are available for ABDAC, the EFED default foliar dissipation half-life of 35 days is used based on high-end dissipation values for pesticides reported by Willis and McDowell (1987).

EECs for terrestrial plants inhabiting dry and wetland areas are derived using TerrPlant (version 1.2.2, October 2009). This model estimates exposure by calculating residues in runoff and in spray drift. These calculations are solely based upon inputs of solubility, application rate, and minimum incorporation depth.

The AgDRIFT spray drift model (v2.1.1; December 2011) is used to assess exposures of organisms to ADBAC that is deposited on terrestrial habitats by spray drift.

Tier I EECs for contact and dietary routes of exposure for foliar and soil applications for honey bees (Apis mellifera) are calculated using the Bee-REX model (version 1.0, October 2015). The Tier I method is intended to generate “reasonably conservative” estimates of pesticide exposure to honey bees, where reliable residue values (i.e., measured residue levels in pollen and/or nectar) are not available. Nectar is considered the major food source for foraging honey bees as well as nurse bees. Therefore, pesticide residues in nectar likely account for most of the exposures to bees, and may represent most of the potential risk concerns for adult bees. However, if residues in pollen are of concern, exposures to nurse bees, which consume more pollen than any other adult honey bees, can be considered. For chemicals with no empirical data to represent the concentration of the chemical in pollen and nectar, dietary exposure for Tier I risk assessment is estimated using generic residue data generated from other chemicals as well as other plant parts. For foliar applications for dietary exposure, it is assumed that pesticide residues on tall grass (from the Kenaga nomogram of T-REX which is incorporated into Bee-REX) are a suitable surrogate for residues in pollen and nectar of flowers that are directly sprayed. For soil applications, pesticide concentrations in pollen and nectar are assumed to be consistent with chemical concentrations in the xylem of barley (calculated using the Briggs’ model). More information on Bee-REX and the methodology associated with estimating

exposure to honey bees is available at EPA's models website (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#terrestrial).

4.4.2 Screening Level Down-the-Drain Analysis

A screening level Down-the-Drain (DtD) analysis would be performed if all of ADBAC's uses were released from residential, commercial, and institutional applications solely to domestic wastewater treatment plants. However, ADBAC is also used in industrial applications that would lead to discharges to industrial wastewater treatment plants. Therefore, no screening level DtD analysis was performed for this PWP.

5 Endocrine Disruptor Screening Program (EDSP)

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision, for ADBAC, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), ADBAC is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[13] and includes some pesticides

[13] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[14]

6 Label Changes

As noted in section 1.5, the Agency is actively working to bring outstanding ADBAC labels into compliance with risk mitigation measures from the ADBAC RED. ADBAC's PDCIs issued in February and March 2015 required revised labels be submitted according to requirements listed in the RED and Fact Sheet. If the Agency finds that ADBAC's product-specific data and labels are not acceptable, the Agency may require the registrant to submit additional or amended information or proceed with suspension action. The Agency will continue to pursue label compliance through regulatory or other action during registration review, as the RED risk mitigation measures (e.g. Table 7) would impact the scope of ADBAC's risk assessment.

As indicated in Section 1.5.1, the Agency has established tolerance exemptions for residues of some uses of quaternary ammonium compounds in/on food (see Table 8). The end-use concentration of all quaternary chemicals in solution is not to exceed 200 or 400 ppm of active quaternary compound. These exemptions are listed under 40 CFR part 180.940. The Agency notes in Section 3.1.1. that some ADBAC labels allow for end-use solution concentrations for food-contact hard surfaces greater than the established tolerance exemption of 200 or 400 ppm; however, the Agency will use the end-use solution concentrations greater than 400 ppm for risk assessment and will evaluate the need for revisions to the product labels and/or to the existing tolerance exemptions.

The Agency invites comment on any label amendments that could be considered to eliminate the anticipated need for EPA to require certain data, reduce the possibility that EPA's planned risk assessments overestimate risk due to reliance on conservative assumptions, and/or improve label clarity.

7 Guidance for Commenters

7.1 Preliminary Work Plan

The public is invited to comment on EPA's Preliminary Work Plan and rationale. The Agency will carefully consider all comments as well as any additional information or data provided in a timely manner prior to issuing a final work plan for the ADBAC registration review case.

7.1.1 Trade Irritants

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. The Agency

[14] http://www2.epa.gov/endocrine-disruption

will work to harmonize tolerances and international maximum residue limits (MRLs) and may modify tolerance levels to do so, when possible. Stakeholders are asked to comment on any trade irritant issues resulting from lack of MRLs or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

7.1.2 Water Quality

The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process*[15] in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

7.1.3 Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to ADBAC compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

7.1.4 Structure Activity Relationships

EPA must rely upon information of appropriate quality and reliability for each decision made by the Agency. In the OPP, the evaluation process for a pesticide chemical traditionally begins with the applicant's submission of a set of studies conducted with the specific pesticide chemical of interest. The use of the results of such testing (measured data) is a logical, scientifically rigorous process that identifies the physical, chemical, and environmental fate properties of the pesticide, as well as the dose and endpoints at which an adverse effect can occur in various animal species.

Today, there is significant interest in alternative techniques, i.e., techniques other than data generation that could significantly inform the Agency's decision-making process. OPP is using the structure activity relationship (SAR) as part of its regulatory decision-making process. In the SAR process, a chemical's molecular structure is compared to that of other chemicals for which data are available. These structural similarities are then used to make predictive judgments about a chemical's physical, chemical, and biological properties. Thus, the chemical's physical, chemical, and biological properties are a function of (or directly related to) the chemical's molecular structure. Quantitative SAR is referred to as QSAR. To develop a QSAR, a selected set of measured data on a single physical, chemical, or biological property is used to derive a model (an equation) to predict the value of that property.

[15] http://www2.epa.gov/pesticide-reevaluation/opp-guidance-submission-state-and-tribal-water-quality-monitoring-data

If stakeholders believe that submission of predicted data can fulfill one of the data needs for the ADBAC case, then the Agency invites submission of this information. The submitter would be expected to supply a rationale describing the utility of the information and provide documentation on the scientific validity of the information. The determination that the predicted data fulfills the data requirement would be at the sole discretion of the Agency. Pre-submission consultation with the Agency is encouraged.

7.1.5 Additional Information

Stakeholders are also specifically asked to provide available information and data that will assist the Agency in refining its risk assessments, including any species-specific ecological effects determinations. The Agency is interested in receiving the following information:

1. Confirmation on the following label information:
    A. Sites of application
    B. Formulations
    C. Application methods and equipment
    D. Maximum application rates
    E. Frequency of application, application intervals and maximum number of applications
    F. Geographic limitations on use
2. Use or potential use distribution
3. Use history
4. Usage/use information for non-agricultural uses (e.g., materials preservation)
5. Typical application interval
6. State or local use restrictions
7. Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
8. Monitoring data

8 Next Steps

After the 60-day comment period closes in November 2016, the Agency will review and respond to any comments received in a timely manner, and then issue a Final Work Plan for the ADBAC case.

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Appendix A Toxicology Profile

Acute Toxicity for Product Labeling

As listed in Table 16, ADBAC is moderately toxic via the oral, dermal and inhalation routes (Category II). Due to the corrosive nature, the primary eye irritation study was waived and given a category I rating. ADBAC is a dermal irritant (category I) but not a dermal or photo sensitizer.

Table 31 – Acute Toxicity Studies for Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC)

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100/ Acute oral toxicity	45109204	=304.5 mg/kg (combined) =510.9 mg/kg (males) =280.8 mg/kg (females)	II
870.1200/ Acute dermal toxicity	45109202	=930 mg/kg (combined) =1100 mg/kg (males) =704 mg/kg (females)	II
870.1300/ Acute inhalation toxicity	44885201	0.054 < < 0.51 mg/L < 0.51 mg/L < 0.51 mg/L	II
870.2400/ Acute eye irritation	waived		I
870.2500/ Acute dermal irritation	45109201	Corrosive	I
870.2600/ Skin sensitization	45109203	Not a dermal sensitizer.	NA
Non-guideline/Photosensitization, guinea pigs	40958501 and supplement 44825002	Not a photosensitizer.	NA

N/A=Not available

Subchronic Toxicity

Adequacy of database for Subchronic Toxicity: subchronic toxicity of ADBAC is considered complete. For oral toxicity, the database includes a 90-day oral toxicity test in rats (MRID 40746601). For dermal toxicity, there is a 21-day dermal toxicity study in guinea pigs (MRID 40700700) and a 90-day dermal toxicity study in rats (MRID 41499601). Inhalation was bridged from DDAC (HASPOC memo TXR 0057356).

870.3100 Subchronic (Oral) Toxicity - Rat

In a subchronic oral toxicity study in rats (MRID #40746601), male and female rats were administered ADBAC (79.7% a.i.) in the diet for 13 weeks at dose levels of 0, 100, 500, 1000, 4000, or 8000 ppm. Increased mortality was observed at the 4000 and 8000 ppm dose groups in both sexes. Decreased body weight, weight gain, food consumption and increased incidence of

microscopic lesions [congestion and edema of the G.I. tract, hemorrhaging of the lungs and brain] were also observed in males and females at 4000 ppm. The Systemic NOAEL for males is 500 ppm and for females is 1000 ppm, based upon decreased body weight and weight gain in males at 1000 ppm, and increased mortality, decreased body weight gain and food consumption, and increased microscopic lesions in female rats at 4000 ppm**.** This study is classified as acceptable.

870.3200 Subchronic (21-day dermal) Toxicity – Guinea pig

In a 21-day dermal toxicity study (MRIDs 40565301 and 41105801), a 1:5 dilution of HSsanitizing carpet shampoo (containing 6% didecyl dimethyl ammonium chloride and 4% alkyl dimethyl benzyl ammonium chloride was applied to a 2 inch square area of the shaved dorsal trunk of 5 male and 5 female guinea pigs at doses of 500 and1000 mg/kg, five days a week, for 21 days. There was no mortality or signs of clinical toxicity noted. Signs of skin irritation were noted during the second week of treatment and the report stated that the response intensified during the third week of treatment. Body weight was decreased in treated males and females by 7% and 11% vs untreated animals at week 3 at 1000 mg/kg. Results of hematology and clinical chemistry measurements indicated a slight elevation of basophils and eosinophils as well as a slight elevation of SGPT and SGOT but statistics were not performed on these data. Histologically, the skin irritation was described as a denuded non-vascularized epidermal layer at the application site.

Although this study was identified with several deficiencies (HED document 007757, from the 1/31/90 review by Pamela Hurley, Ph.D.), the data are useful for determining a level of concern for dermal irritation and systemic effects after short-term exposure to ADBAC. In this case, the 500 mg/kg dose level produced no significant dermal or systemic effects, and is considered a NOAEL for the study for dermal irritation and systemic effects.

870.3250 Subchronic (90-day dermal) Toxicity – Rat

In a 90-day dermal toxicity study (MRID 41499601), ADBAC (81.09% a.i.) was applied at dose levels of 0, 2, 6, or 20 mg/kg/day to the clipped backs of Sprague-Dawley rats for 68 hours per day, 5 days per week, for 13 weeks. Although higher doses were tested in a preliminary range-finding study (6, 20, 60, 120, and 200 mg/kg/day), the high dose selected for the main study (20 mg/kg/day) was chosen on the basis that higher concentrations produced skin irritation that was considered greater than slight.

A significant dose related decrease in reticulocyte count was observed in the 6 and 20mg/kg/day females. Decreases in reticulocyte count are normally associated with regenerative responses to anemia. However, no evidence of anemia was seen in other hematological parameters. Furthermore, the decreased levels in treated females were similar to the levels observed in control males. Thus, the decreasing reticulocyte count was most likely not a biologically significant finding.

A significant increase in hyperkeratosis was observed in treated skin of high dose females, but this lesion was also observed in increased incidence in male rats at all doses including controls.

The NOAEL for dermal effects and the NOAEL for systemic effects were 20 mg/kg/day.

TG412 Subchronic (28-day inhalation) Toxicity – Rat – DDAC

In a subchronic inhalation toxicity study (MRID 48667903), Didecyl dimethyl ammonium chloride (DDAC) (50.79%, 00503J5) was administered to 5 Sprague-Dawley rats/sex/concentration by dynamic nose-only exposure at concentrations of 0, 0.08, 0.5, and 1.5 mg/m^3 (0.00008, 0.0005, 0.0015 mg/L) for 6 hours/day, 5 days/week for a total of 20 or 21 days depending on necropsy time. There were two additional groups of 5 rats/sex exposed to 0 or 1.5 mg/m^3 which had a 2-week recovery period before necropsy.

No early mortality was observed in any of the dose groups. At all concentrations in males and at the 0.5 and 1.5 mg/m^3 concentrations in females, lower body weight was observed. In males, these body weights were 6.1%, 9.9% and 20.5% lower respectively in males and 4.0% and 8.5% lower respectively in females. This was statistically significant in 1.5 mg/m^3 dosed males. Lower body weight was correlated with statistically significant lower food consumption. In the 1.5 mg/m^3 group, females and males had increased body weight gain during recovery, leading to full resolution of body weight reduction in females and partial resolution in males.

Concentration-related higher lung weights per 100 grams of body weight occurred in the 1.5 mg/m^3 group males and 0.5 and 1.5 mg/m^3 group females. These changes were reversible. Ulceration of the stratified squamous epithelium in the nasal cavity in the 1.5 mg/m^3 group male and females and degeneration of the olfactory epithelium of the nasal cavity in the 0.5 and 1.5 mg/m^3 group males and 1.5 mg/m^3 group females also occurred.

The bronchoalveolar lavage fluid (BALF) analysis indicated that at the high dose (for most measures the only dose examined other than control) that neutrophils and eosinophils increased with a concomitant decrease in macrophages. In males, there was an increase in cell count and total protein across all doses. In females there was a dose-dependent increase in LDH across all doses, while in males there were increases but the size of some standard deviations made determining dose dependence difficult. This increase was consistent with an increase in lung inflammation. Statistical significance was difficult to assess with the small sample size of 5 animals per group, but trends towards changes in these parameters was clear.

Ulceration and increase in mucus production was most pronounced in the rostral section of the nasal cavity. DDAC produced ulceration of the nasal vestibule lined with stratified squamous epithelium and increased mucus production. There was also degeneration of the olfactory epithelium along with squamous metaplasia in nasal sections II and III. These regions are especially susceptible to injury, as they represent the most rostral extension of the olfactory epithelium. There were increases in mucus respiratory epithelium in a dose and severity dependent fashion. There were also changes in nasal cavity hemorrhage. These effects generally change in severity with dose.

The LOAEC is 0.08 mg/m^3/day based on increases in relative lung weight (males), changes in LDH, BALF total protein, BALF cell count (males only), increase in mucus in the respiratory epithelium, increase in hemorrhage, increase in mucoid exudate. These effects are observed to

occur in a dose dependent fashion. The changes in BAL fluid are consistent with inflammatory effects in the lung. There was also the start of a trend towards lower body weights in males at this dose. There is no NOAEC established in this study.

The RDDR is 0.298 for Extrathoracic Effects based on the MMAD of 1.5 microns and GSD of 1.83 at the dose of 0.08 mg/m^3 and a rat body weight of 289 gram. The rat body weight is the average of the male and female rats of the 0.08 mg/m^3 dose group at Day 25.

The HEC is 0.018 mg/m^3 for 8 hour daily exposures based on the following**:**
HEC = LOAEC * (6 hours/day Rat Exposure /8 hours/day Human Exposure) * RDDR

These findings and conclusions were made using the available information within the report.

This study was missing histopathology of numerous major organ groups as required by the guideline, including but not limited to heart, thymus, spleen, thyroid, bone, testes and stomach. Although these measurements were not made, per guideline, this study is considered acceptable as this study was designed to examine route specific (primarily respiratory) effects.

The study is well designed and provides scientifically sound information. The study is classified as acceptable.

Developmental Toxicity

Adequacy of database for Prenatal Developmental Toxicity: The database includes 2 developmental studies, one in the rat (range-finding MRID 42645101 and main study MRID 42351501) and another in the rabbit (range-finding MRID 42734401 and main study MRID 42392801).

870.3700a Prenatal Developmental Toxicity (Gavage) Study – Rat

In a dose range-finding study for developmental toxicity in rats (MRID # 42645101), ADBAC (81.09%) was administered at doses of 0, 25, 50, 100, 200, or 400 mg/kg/day to CD rats (5/dose) by oral gavage on gestation days 6 through 15, inclusive. Doses ≥ 200 mg/kg/day resulted in 100% mortality; necropsy findings revealed a distended and change in color of the stomach, and distended intestines filled with mucoid fluid. These dams also exhibited clinical signs including loose feces, perioral wetness and perioral encrustation, ataxia, hypoactivity, urogenital area wetness, and audible respiration. Maternal toxicity observed at 100 mg/kg/day was manifest as significantly increased incidence of perioral wetness. The maternal NOAEL and LOAEL are 50 and 100 mg/kg/day, respectively. The NOAEL for developmental toxicity is 100 mg/kg/day based on no survival of dams at 200 and 400 mg/kg/day.

In a developmental toxicity study in rats (MRID # 42351501), female Sprague-Dawley rats (25/dose) were administered ADBAC (81.09% a.i.) by gavage at doses of 0, 10, 30, and 100 mg/kg on gestation days 6 through 15 inclusive for assessment of developmental toxicity. There was no mortality in maternal animals observed at any dose level. At 100 mg/kg/day, one dam exhibited dehydration, unkempt appearance, loose feces, and perioral wetness. At 30 mg/kg/day,

one dam was noted with perioral wetness, gasping, loose feces, and urine stains. Decreased body weight gain (12-13%) was observed in maternal animals at 30 mg/kg/day during gestation days 6- 15. Food consumption was not consistently affected by treatment. There were no treatment related increases in the incidence of fetal external, visceral, or skeletal abnormalities at any dose level. Based on the results of this study, the Maternal NOAEL is 10 mg/kg/day, and the Maternal LOAEL is 30 mg/kg/day, based on clinical signs and decreased body weight gain. The Developmental toxicity NOAEL is 100 mg/kg/day, and the Developmental toxicity LOAEL is > 100 mg/kg/day. There was no evidence for developmental toxicity of ADBAC in this study. This study is classified as acceptable.

870.3700b Prenatal Developmental Toxicity (Gavage) – Rabbit

In a dose range-finding study for developmental toxicity in rabbits (MRID # 42734401), ADBAC (81.09%) was administered at doses of 0, 1, 3, 10, 30, or 60 mg/kg/day to pregnant New Zealand White rabbits (5/dose) by oral gavage on gestation days 6 through 18. Mortality was observed at doses of 30 and 60 mg/kg/day (2 and 5 does, respectively). Audible respiration was observed at doses greater than or equal to 10 mg/kg/day. At doses greater than or equal to 30 mg/kg/day, clinical signs included hypoactivity, perioral wetness, and labored breathing. At 60 mg/kg/day, clinical signs included paralysis, cold extremities, prostration, slow respiration, emaciation, loose feces, and perioral encrustation. Decreased body weight gain and food consumption were observed at doses greater than or equal to 10 mg/kg/day. Developmental toxicity was not observed at any of the doses tested. The maternal NOAEL for the range-finding study is 3 mg/kg/day and the LOAEL is 10 mg/kg/day, based on clinical signs and reduced body weight gain and food consumption. There was no evidence of developmental toxicity of ADBAC in this study.

In a developmental toxicity study in rabbits (MRID # 42392801), ADBAC (81.09%) was administered at doses of 0, 1, 3, or 9 mg/kg/day to pregnant New Zealand White rabbits 16/dose) by oral gavage on gestation days 6 through 18, inclusive. There was no mortality or abortions at any dose level. Hypoactivity and labored breathing were observed at 9 mg/kg/day in 2 of 15 rabbits. There were no effects on maternal body weight, food consumption, cesarean section observations, or necropsy observations. In offspring, there was no evidence of developmental toxicity at any dose level tested. The Maternal NOAEL is 3 mg/kg/day, and the Developmental NOAEL is 9 mg/kg/day. The Maternal LOAEL is 9 mg/kg/day, based on clinical signs of toxicity, and the Developmental LOAEL is > 9 mg/kg/day. There was no evidence of developmental toxicity of ADBAC in this study. This study is classified as acceptable.

Reproductive Toxicity

Adequacy of database for Reproductive: The database for reproductive toxicity of ADBAC is considered complete. The database includes an acceptable 2-generation reproduction toxicity study in rats, MRID 41385001.

870.3800 Reproduction and Fertility Effects – Rat

In a two-generation reproduction toxicity study in rats (MRID # 41385001), ADBAC (81.09%) was administered in the diet to groups of male and female Sprague-Dawley rats (28/sex/dose) at dose levels of 0, 300, 1000, or 2000 ppm over two generations. After 10 weeks of dietary treatment, F0 parental animals were mated. F1 parental animals were mated after 15 weeks of dietary treatment. Mean compound consumption was 20.7, 68.2, and 134.7 mg/kg/day for F0 males, and 25.5, 81.3, and 164.7 mg/kg/day for F0 females. For the F1 males, mean compound consumption was 19.1, 62.5, and 125.4 mg/kg/day, and 24.8, 78.5, and 157.1 mg/kg/day for F1 females.

There was no treatment-related mortality in parental animals at any dose level, and there were no reported signs of clinical toxicity in parental animals. Although some decrease in body weight was observed in both generations at the top dose, the significant variability observed did not qualify this as a treatment-related effect.

In pups of both generations, mean body weights at the top dose were significantly reduced during lactation and post-weaning periods. There were no adverse effects noted on gestational length, mating, fertility, or other gestational indices.

Based on the results of this study, the Parental NOAEL = 146 mg/kg/day, and the Parental LOAEL > 146 mg/kg/day (highest dose tested). The Developmental/Systemic NOAEL = 65.4/79.9 mg/kg/day (M/F), and the Developmental /Systemic LOAEL = 130.1/160.9 mg/kg/day (M/F), based on reduced pup body weight and weight gain during lactation [doses for both the F0 and F1 pups combined].

This study is classified as acceptable.

Chronic Toxicity

Adequacy of database for Chronic Toxicity: The database for chronic toxicity of ADBAC is considered adequate, including a chronic toxicity study in dogs (MRID 43221101) and a combined chronic oral toxicity/carcinogencity study in rats (MRID 41947501).

870.4100 Chronic Toxicity (Oral) – Dog

In a chronic toxicity study in dogs (MRID 43221101), groups of 4 male and female beagle dogs per group received either 0, 120, 400, or 1200 ppm (0, 3.79, 13.1, or 33.8 mg/kg/day in males and 0, 3.67, 14.6, or 38.6 mg/kg/day in females) alkyl dimethyl benzyl ammonium chloride [ADBAC, 80% a.i.] as a direct dietary admix for one year. Systemic toxicity was observed at 400 ppm and above in female dogs and at 1200 ppm in males as reduced body weight gain (approximately 10% reduction) after 52 weeks of exposure. Food consumption was decreased in the 1200 ppm males and females for the entire study period (approximately 15% reduction in males and 5% reduction in females). Based on the data in this study, the Systemic Toxicity NOAEL was 120 ppm (3.79 mg/kg/day in males, 3.67 mg/kg/day in females) and the LOAEL was 400 ppm (13.1 mg/kg/day in males, 14.6 mg/kg/day in females) based on reduced body weight gain.

870.4300 Chronic Toxicity/ Carcinogenicity (Oral) – Rat

In a chronic toxicity / carcinogenicity study (MRID # 41947501), ADBAC (81% purity) was administered in the diet to groups of male and female Sprague-Dawley rats (50/sex/dose) at dose levels of 0, 300, 1000, and 2000 ppm (nominal doses of 13, 44, and 88 mg/kg/day in males; 17, 57, and 116 mg/kg/day in females) for 104 weeks. Significant decreases in group mean body weight were observed in male rats at the 2000 ppm dose level during weeks 1-26 of the study and then sporadically thereafter. Body weights of high dose female rats were also significantly decreased during weeks 1-60 of the study. Body weight gain was decreased 11% on average in high dose males and 14% in high dose females. There were no significant treatment-related effects on clinical chemistry, hematology, or urinalysis. No treatment-related non neoplastic gross or microscopic lesions were evident in any of the treated groups of rats. There was no evidence of carcinogenicity of ADBAC in this study. The Systemic toxicity NOAEL = 1000 ppm, (44 mg/kg/day [M]; 57 mg/kg/day [F]), and the Systemic toxicity LOAEL = 2000 ppm (88 mg/kg/day [M]; 116 mg/kg/day [F], based on decreased body weight and weight gain. This study is classified as acceptable and satisfies the guideline requirement for a chronic toxicity / carcinogenicity study in rats.

Carcinogenicity

Adequacy of database for Carcinogenicity: The database for the carcinogenicity of ADBAC is considered adequate. The database for carcinogenicity includes the 104 week chronic toxicity/carcinogenicity study in rats (MRID 41947501) described in 4.5 and an additional carcinogenicity study in the mouse (MRID 41765201). Results of both studies showed ADBAC to be negative for carcinogenicity.

870.4200 Carcinogenicity (Oral) – Mouse

In a carcinogenicity study in mice (MRID # 41765201), ADBAC (81% purity) was administered in the diet to male and female CD-1 mice (60 sex/dose) at levels of 0, 100, 500, or 1500 ppm for 78 weeks (nominal doses of 14.9, 73.4 and 229.3 mg/kg/day in males; 17.8, 92.1 and 288.6 mg/kg/day in females). No significant differences in the incidence of mortality were observed in treated animals versus controls. No clinical signs of toxicity were observed at any dose level tested. Significant reductions in group mean body weight were observed at the high dose in male and female mice throughout the treatment period with no significant reduction in food intake. There were no significant treatment-related effects on organ weights, macroscopic, or microscopic pathology in treated mice at any dose level. ADBAC was negative for carcinogenicity in this study. The Systemic LOAEL = 1500 ppm in male and female mice (229.3 / 288.6 mg/kg/day), based on reduced body weight. The Systemic NOAEL = 500 ppm in male and female mice (73.4 / 92.1 mg/kg/day). This study is classified as acceptable and satisfies the guideline requirement for a carcinogenicity study in mice.

Mutagenicity

ADBAC has been tested for mutagenicity in an HGPRT assay in CHO cells for forward mutations (MRID 41012701), an in vivo bone marrow chromosome aberration assay (MRID

40311101, supplemental MRID 43037701), and an unscheduled DNA synthesis assay (MRID 42290802 and 4229080). Results of all of these studies were negative for ADBAC.

Metabolism

Adequacy of database for Metabolism and Pharmacokinetics: Disposition of ADBAC was examined in male and female Sprague-Dawley rats (MRID 40990701, supplemental MRIDs 41087701 and 44783401) following a 10 mg/kg single dose by the oral or intravenous route, following exposure to 100 ppm ADBAC for 14 days in the diet, or after a single oral dose of 50 mg/kg. Ring-labeled test material was used. Following oral administration, from 5-8% of the administered dose was eliminated in urine and 90-98% in feces. No apparent differences in disposition were noted between sexes. Following intravenous administration, males eliminated 31% of the dose in urine and 44% in feces, while females eliminated 21% in urine and 55% in feces following intravenous administration. After oral administration, from 0.03-0.58% of the administered dose was accounted for in tissues. After intravenous administration, tissue residues accounted for 33-36% of the dose and were observed mainly in the carcass. The results of this study indicate that a majority of an administered dose of ADBAC is eliminated in feces and involves biliary excretion.

Other Toxicological Effects

Immunotoxicity, acute and subchronic toxicity studies were waived (HASPOC memo TXR# 0057356).

Appendix B Environmental Fate

Environmental Fate and Transport Properties of ADBAC

ADBAC is completely soluble in water and, based on the vapor pressure and Henry's Law values (Table 4), is not expected to partition from soil and water into air. ADBAC is stable to hydrolysis at pH values of 5, 7, and 9, stable to photodegradation in pH 7 buffered aqueous solutions, but degraded in water in the presence of a photosensitizer with a half-life of 7.1 days.

Test data indicate that ADBAC would be expected to be amenable to both sorption and biodegradation. The high log Kow of 3.91 (Table 4) indicates that ADBAC is relatively hydrophobic, partitioning more to octanol than to water. Log Koc values of greater than 6 (MRIDs 40835605 and 42414801) indicate that ADBAC would be expected to be immobile due to strong sorption to soil and sediment. In aqueous media offering the potential for both sorption and biodegradation, there is conflicting information about which of these processes would be expected to predominate. Based on results of aerobic and anaerobic aquatic metabolism studies (MRID 40835604, 41105501, 42415101), ADBAC was indicated to be stable to microbial degradation under aerobic conditions and anaerobic conditions in water and sediment, indicating that sorption would predominate. In contrast, results of a ready biodegradability study met key criteria that indicated that ADBAC appears to be readily biodegradable (MRID 46865601) based on 10% of the theoretical maximum quantity of CO_2 ($ThCO_2$) formation by 6 days and >60 % of $ThCO_2$ before day 13 (within 10-day window); 95.5% of ADBAC biodegraded after 28 days, indicating that biodegradation would predominate over sorption.

A possible explanation of these apparently conflicting indications about whether sorption or biodegradation of ADBAC would predominate is the difference between the test media used in the ready biodegradability study and the aquatic metabolism studies. The stability of ADBAC in the aerobic and anaerobic aquatic metabolism studies can be attributed to strong sorption of ADBAC to sediment present in a test medium that allows for both sorption and microbial degradation. In contrast, the finding of ready biodegradability of ADBAC in the ready biodegradability study can be attributed to the influence of biodegradation which occurred in a medium in which microorganisms present are acclimated to experimental conditions that are typical of wastewater treatment plants. Consequently, these conditions would be expected to favor biodegradation over sorption of ADBAC.

There is uncertainty about whether sorption or biodegradation of ADBAC would predominate during wastewater treatment. In the absence of data on the extent for ADBAC to sorb to sludge biomass during wastewater treatment, data from an Activated Sludge Sorption Isotherm (ASSI) study (GLN 835.1110) are needed. If the results from this study do not indicate a high potential for ADBAC to sorb to sludge biomass, the Agency may require additional information on the ready biodegradability study (MRID 46865601) submitted to the Agency so it can be upgraded to an acceptable status. If results from the ASRI study, however, indicate high toxicity to activated sludge microorganisms (EC_{50} less than or equal to 20 mg/L), the Agency may require a

wastewater treatment plant biodegradation simulation test rather than a ready biodegradability test.

Data relevant to soil metabolism have not been submitted. In the ambient environment, sorption to soil, sediment, and sludge is expected to be the primary transformation process for ADBAC based on the fact that this is a quaternary ammonium compound with a positive electrical charge that will sorb to negatively-charged particles. In soil and sediment, ADBAC is expected to be immobile based on the Freundlich K_{ads} values of 5,123 to 32,429 L/kg and K_{oc} values of 640,389 to 6,171,657 L/kg (MRID 40835605 and 42414801) based on the FAO soil mobility classification system. Because of its strong sorption to soils, ADBAC is not expected to leach to ground water or be present in dissolved form in runoff water discharged to surface water. ADBAC, however, is expected to be associated with the eroded sediment that is transported during runoff. Table B1 contains a summary of environmental fate data for ADBAC.

ADBAC has the potential to reach WWTPs from the registered uses, and data on activated sludge sorption isotherm (OCSPP 835.1110) and activated sludge respiration inhibition (OCSPP 850.3300) have not been submitted and are required.

Water and Sediment

Hydrolysis

In an acceptable hydrolysis study (MRID 40835602), ADBAC was essentially stable with half-lives of 150 days at pH 5, 183 days at pH 7, and 379 days at pH 9.

Aqueous Photolysis

In a photodegradation in water study (MRID 40835603), ADBAC was found to be stable to photodegradation in sterile buffer solution at pH 7 at 25^{o}C; however, in a sensitized solution ADBAC degraded with a half-life of 7.1 days. This study was classified as upgradable because an unidentified degradate was found 30 days post treatment; however, the study is not invalidated because ADBAC is expected to sorb strongly to sediment, and photodegradation is not expected to be a significant degradation route. Further, ADBAC does not absorb UV light in the 290-800 nm wavelength (MRID 47398502).

ADBAC is considered stable to photodegradation and the aqueous photolysis data may be used in a risk assessment. No further aqueous photolysis data are anticipated to be required.

Octanol-Water Partition Coefficient and Bioconcentration in Fish

The log K_{ow} of ADBAC is 3.91 (Table 4), which is above the level of concern for potential bioconcentration in fish (>3). However, the submitted bioconcentration in fish study (MRID 41026801) demonstrated limited bioconcentration factors of 33X (edible tissues), 160X (non-edible tissue), and 79X for whole fish. The limited bioconcentration is consistent with miscibility of ADBAC in water (Table 4). No additional data are anticipated to be required for bioconcentration in fish.

Aerobic Aquatic Metabolism

In an acceptable aerobic aquatic metabolism study (MRID 40835604), ADBAC showed no degradation during the 30-day study and is classified as stable. There are indications that strong sorption to sediment contributed to this apparent stability.

Anaerobic Aquatic Metabolism

In an acceptable anaerobic aquatic metabolism study (MRIDs 41105501 and 42415101), the half-life of ADBAC was determined to be 1,815 days; ADBAC is considered stable. There are indications that strong sorption to sediment contributed to this apparent stability.

Leachability from Treated Wood

Wood leaching data were not submitted for ADBAC, but based on the structural, chemical, and physical similarities, DDAC leaching data were used as a surrogate. The leaching rates for DDAC were essentially proportional to the treatment rate of the cubes. The maximum, minimum, and average leaching rates ranged from 1,219-13,330, 104-497, and 348-3,737 ug/cm^2/day at 0.8-3.2 % w/w. The total amount of DDAC leached ranged from 2.6-8.2 % (MRID 49812403). The Agency anticipates similar leaching rates for ADBAC.

Soil

Soil Leaching Adsorption/Desorption Batch Equilibrium

ADBAC had Freundlich K_{ads} value range from 5,123 – 32,429 L/kg and $K_{oc\ values}$ of 640,389 – 6,171,657 L/kg (MRID 40835605 and 42414801). ADBAC is expected to be immobile based on its Freundlich K_{ads} and K_{oc} values. Additional soil leaching data are not anticipated to be required.

Aerobic/Anaerobic Soil Metabolism

No soil metabolism data are anticipated to be required for antimicrobial uses; however, soil metabolism data are anticipated to be required for conventional uses. The data will allow EPA to evaluate potential aquatic exposure of ADBAC and its degradates via runoff from soil erosion after ADBAC has been applied to lawns, turf, and golf courses.

Fate and Transport in WWTP

Activated Sludge Respiration Inhibition

ASRI data are anticipated to be required because the registered uses of ADBAC can result in exposure to microorganisms in WWTPs.

Activated Sludge Biodegradation

In a ready biodegradability study (MRID 46865601), ADBAC was reported to be readily biodegradable based on 10% of the theoretical maximum quantity of CO_2 ($ThCO_2$) formation by

6 days and >60 % of $ThCO_2$ before day 13 (within 10-day window). The study results indicated that ADBAC biodegradation reached 95.5% after 28 days. This study, however, was classified as upgradable rather than acceptable because it did not contain some key information that would allow the Agency to verify these results.

Activated Sludge Sorption Isotherm

The results of the adsorption/desorption study indicate that ADBAC has a high potential to sorb in a wide range of environmental conditions. No data are available; however, on the potential for ADBAC to sorb during wastewater treatment. ASSI data are anticipated to be required because the registered uses of ADBAC can result in releases to WWTPs and the log K_{ow} value is ≥3. Results of the adsorption/desorption study indicate high sorption potential, and ADBAC is a quaternary ammonium compound that is expected to sorb to sludge because of its positive electrical charge.

If the ASSI study does not demonstrate a strong potential to sorb during activated sludge treatment, the Agency may require verification of results from the ready biodegradability study (MRID 46865601) or an appropriate WWTP biodegradability study as determined by the results of the ASRI test.

Table B1. Environmental Fate Properties of ADBAC

Guideline No.	Parameter	ADBAC	MRID
Leaching-Adsorption/Desorption			
835.1240	K_f/K_{oc} (L/kg) (sand, silt loam, sandy loam, clay loam)	Kf (Koc) 6,172 ($6.2x10^6$), 10,797 ($2.2x10^6$), 5,123 ($6.4x10^5$), 32,429 ($1.7x10^6$)	40835605 42414801
Persistence in Water (half-life)			
835.2120	Hydrolysis at 25 °C (days) pH 5, pH 7, pH 9	150 d, 183 d, 379 d	40835602
835.2240	Aqueous photolysis at 25 °C (days)	stable	40835603
835.4300	Aerobic aquatic metabolism (days)	Stable (sandy loam)	40835604
835.4400	Anaerobic aquatic metabolism half-life (days)	1,815 d (sandy loam)	41105501
Persistence in WWTP (% removed)			
835.3110	Ready Biodegradability	<10% at 24 hrs, 98.5% at 28 d	46865601

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Appendix C Ecotoxicology Profile

Toxicity to Terrestrial Animals

Birds

Results of the available acute oral (850.2100) and dietary (850.2200) toxicity studies are provided in Table C1. No additional avian toxicity data are needed for the antimicrobial uses. To support the conventional uses, an avian acute oral toxicity study with a passerine species (850.2100) and avian reproduction toxicity studies on an upland game species and a waterfowl species (850.2300) are anticipated to be required.

Table C1. Acute Oral and Dietary Toxicity of ADBAC to Birds

Species	% ai	Toxicity	Toxicity Category	Status/ MRID
Northern bobwhite (*Colinus virginianus*	81	LD_{50} = 136 mg/kg bw	Moderately toxic	Acceptable 42885901
	80	LD_{50} = 220 mg/kg bw	Moderately toxic	Acceptable 00122144
	80	LC_{50} >2430 ppm	Slightly toxic at most	Supplemental 00104009
	80	LC_{50} =2565 ppm	Slightly toxic	Supplemental 00119707
	80	LC_{50} >5000 ppm	Practically nontoxic	Acceptable 00065213
	5	LC_{50} >5000 ppm	Practically nontoxic	Supplemental 00101864
Mallard (*Anas platyrhynchos*)	80	LD_{50} = 580 mg/kg bw	Slightly toxic	Acceptable 00122145
	80	LC_{50} >5000 ppm	Practically nontoxic	Acceptable 00065212
	80	LC_{50} >5760 ppm	Practically nontoxic	Supplemental 00104008
	80	LC_{50} >4500 ppm	Slightly toxic at most	Supplemental 00119707
	5	LC_{50} >5000 ppm	Practically nontoxic	Supplemental 00101864

Nontarget Insects - Honeybees

For antimicrobial uses, no data are available. Additional data are anticipated to be required to support ADBAC antimicrobial uses as a wood preservative and conventional uses. These data include acute oral toxicity to adult honey bees (non-guideline), acute oral toxicity to larval honey bees (non-guideline) and chronic toxicity to adult honey bees (non-guideline). Higher-tier colony level studies may be required pending the outcome of the screening level assessment using

laboratory-based acute (single dose) and chronic (repeat dose) toxicity studies with adult and larval bees (all with TGAI). These higher-tier studies include field trial of residues in pollen and nectar (850.3030), semi-field testing for pollinators (TEP) and field testing for pollinators (TEP). In addition, although the acute contact toxicity to adult honey bees study (850.3020) was submitted, there is still outstanding data that must be submitted.

Terrestrial Plants

No data for terrestrial plants are available for ABDAC. Tier I and Tier II seedling emergence (850.4100 and 850.4225) and vegetative vigor data (850.4150 and 850.4250) with the TEP are anticipated to be required to support the conventional uses.

Toxicity to Aquatic Animals

Freshwater Fish and Invertebrates, Acute

Results of acute testing with cold-water and warm-water freshwater fish (850.1075) and freshwater invertebrates (850.1010) are presented in Table C2. No additional data are anticipated to be required for the antimicrobial or conventional uses.

Table C2. Acute Toxicity of ADBAC to Freshwater Fish and Invertebrates

Species	% ai	96-h LC_{50} (µg /L)	Toxicity Category	Status/ MRID
Fathead minnow (*Pimephales promelas)*	81.9	280	Highly toxic	Supplemental 43740103
	50	390	Highly toxic	Supplemental Dobbs et al. 1995*
	50	980	Highly toxic	Supplemental 00064897
Bluegill sunfish (*Lepomis macrochirus)*	50	320	Highly toxic	Supplemental 00064897
	50	510	Highly toxic	Supplemental 00119694
	95.5	515	Highly toxic	Acceptable 41947201
	80	2710	Moderately toxic	Supplemental 00058836
Rainbow Trout (*Oncorhynchus mykiss)*	95.5	923	Highly toxic	Acceptable 41947202
	50	1010	Moderately toxic	Supplemental Dobbs et al. 1995*
	80	1250	Moderately toxic	Acceptable 00122146

Species	% ai	96-h LC_{50} (µg /L)	Toxicity Category	Status/ MRID
	50	2450	Moderately toxic	Supplemental 00064897
	80	7690	Moderately toxic	Supplemental 00058836
Brown trout (*Salmo trutta*)	50	1950	Moderately toxic	Supplemental 00064897
Channel catfish (*Ictalurus punctatus*)	50	980	Highly toxic	Supplemental 00064897
Brown bullhead *(Ictalurus nebulosus*)	50	1590	Moderately toxic	Supplemental 00064897
Green sunfish (*Lepomis cyanellus*)	50	2250	Moderately toxic	Supplemental 00064897
Redear sunfish (*Lepomis microlophus*)	50	740	Highly toxic	Supplemental 00064897
Smallmouth bass (*Micropterus dolomieui*)	50	1370	Moderately toxic	Supplemental 00064897
Goldfish (*Carassius auratus*)	50	1490	Moderately toxic	Supplemental 00064897
Lake trout (*Salvelinus namaycush*)	50	420	Highly toxic	Supplemental 00064897
Largemouth bass ((*Micropterus salmoides*)	50	1130	Moderately toxic	Supplemental 00064897
Waterflea (*Daphnia magna)*	95.5	5.9	Very highly toxic	Acceptable 41947203
	50	20	Very highly toxic	Supplemental Dobbs et al. 1995*

* Study was reviewed by OPP but not assigned an MRID number.

Estuarine/Marine Organisms, Acute

The available data for estuarine/marine fish (850.1075), bivalves (850.1055), and shrimp (850.1035) are presented in Table C3. No additional data are anticipated to be required for the antimicrobial or conventional uses.

Table C3. Acute Toxicity of ADBAC to Estuarine/Marine Organisms

Species	% ai	96-h LC_{50} (µg /L)	Toxicity Category	Status/ MRID
Sheepshead minnow (*Cyprinodon variegatus*)	80.8	860	Highly toxic	Acceptable 42479502
	50	880	Highly toxic	Supplemental Dobbs et al. 1995*
Inland silverside (*Menidia beryllina*)	50	310	Highly toxic	Supplemental Dobbs et al. 1995*
Eastern oyster (*Crassostrea virginica*)	80.8	55	Very highly toxic	Supplemental 42479503
Mysid shrimp (*Mysidopsis bahia)*	80.8	92	Very highly toxic	Acceptable 42479501
	50	>170	Not determined	Supplemental Dobbs et al. 1995*
Grass shrimp (*Palaemonetes pugio*)	80	2810	Moderately toxic	Acceptable 00122147
Shore crab (*Pachygrapsus crassipes*)	80	21,600	Slightly toxic	Acceptable 00122148

* Study was reviewed by OPP but not assigned an MRID number.

Aquatic Organisms, Chronic

Chronic toxicity tests are available for freshwater fish (early life stage, 850.1400) and freshwater invertebrate (life cycle, 850.1300) (Table C4). Acute:chronic ratios can be used to estimate the chronic toxicity of the ADBACs to estuarine/marine fish and invertebrates. No additional testing are anticipated to be required for the antimicrobial or the conventional uses.

Table C4. Chronic Toxicity of ADBAC to Freshwater Organisms

Species	% Active Ingredient	NOAEC and LOAEC (µg /L)	Status/ MRID
Fathead Minnow (*Pimephales promelas*)	30	NOAEC = 32.2 LOAEC = 75.9	Acceptable 42302102
Waterflea (*Daphnia magna*)	30	NOAEC = 4.15 LOAEC = not determined	Supplemental 42302101

Benthic Invertebrates, Chronic

ADBACs have a strong tendency to bind to sediment/soil (K_{ads} >5000, K_{oc} >600,000) and chronic exposure to benthic invertebrates is expected. One chronic sediment toxicity study (no guideline no.) is available for the midge (Table C5). This study partially fulfills the need for chronic sediment testing for freshwater species. To support the antimicrobial and conventional uses, chronic studies also are anticipated to be required for a freshwater amphipod (*i.e., Hyalella azteca*) and an estuarine/marine amphipod (*i.e., Leptocheirus plumulosus*).

Table C5. Chronic Toxicity of Sediment-Incorporated ADBAC to Freshwater Invertebrates

Species	% ai	Endpoints (mg/kg sediment)	Status/ MRID
Midge (*Chironomus tentans*)	80	28-d NOAEC = 520 28-d LOAEC = 1200 14-d LC50 = 548	Supplemental 43731101

Toxicity to Aquatic Plants

No valid guideline data (850.4400, 850.4500, and 850.4550) are available. To support the antimicrobial and conventional uses, testing is anticipated to be required with one species of aquatic vascular plant (*Lemna gibba*) and four species of algae and cyanobacteria: (1) freshwater green alga, *Selenastrum capricornutum,* (2) marine diatom, *Skeletonema costatum,* (3) freshwater diatom, *Navicula pelliculosa,* and (4) cyanobacteria, *Anabaena flos-aquae.*

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Appendix D Screening Level Down-the-Drain Analysis

No screening level Down-the-Drain (DtD) assessment was performed for this PWP. A rationale is provided in Section 4.4.2.